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SYMPOSIUM ON BRAIN AND MIND

NOTES ON CORTICAL EVOLUTION

GERHARDT VON BONIN, M.D.
CHICAGO

A COMPLETE account of the phylogenesis of the cerebral cortex is clearly far beyond what can be achieved in the short time that is at my disposal. It would, moreover, hardly be germane to the main topic of this symposium, the relation of brain and mind. But to point to some of the structural and functional changes which took place in the evolution of the primates is eminently suitable as a "curtain raiser."

To write the story of the evolution of the primate brain, as T. Edinger [1] did for the horse, is, in fact, not possible at present, since we have far too few fossil records. We can compare only living forms, and the limitations inherent in this procedure are obvious.[2] We know that primate brains of about the same size differ but little from each other, regardless of the genus to which its bearer belongs. Thus, Cebus and Macaca have brains which are as difficult to distinguish as those of a lion and a tiger.[3] The case of Ateles and Hylobates appears to be slightly different, but that may be due to the high specialization which the development of a prehensile tail imposed upon the brain of the former.[4] Despite this exception, we may assume as a working hypothesis that all primate brains are models of each other, on different scales, in the sense defined long ago by Isaac Newton in his theory of similitude.[2]

Let us begin, then, by contrasting the primate with the nonprimate cortex. That primates are microsomatic, i. e., have a small rhinencephalon, is a familiar statement of comparative neurology [5]; I need not dwell upon it here. It may be pointed out in passing, however, that the septal and parolfactory region, which L. Edinger [6]

From the Department of Anatomy, University of Illinois School of Medicine.

Read at the Seventy-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 18, 1951, as part of a Symposium on the Brain and the Mind.

1. Edinger, T.: Evolution of the Horse Brain, Memoir No. 25, The Geological Society of America, 1948, p. 177.

2. von Bonin, G.: Types and Similitudes, Philos. Sc. **13**:196-202, 1946.

3. Connolly, C. J.: External Morphology of the Primate Brain, Springfield, Ill., Charles C Thomas, Publisher, 1950.

4. Fulton, J. F., and Dusser de Barenne, J. G.: Representation of the Tail in the Motor Cortex of Primates, with Special Reference to Spider Monkeys, J. Cell. & Comp. Physiol. **2**:399-425, 1933.

5. Edinger, L.: Vorlesungen über den Bau der nervösen Zentralorgane des Menschen und der Tiere, Leipzig, F. C. W. Vogel, 1911. Ariëns Kappers, C. U.; Huber, G. C., and Crosby, E. C.: Comparative Anatomy of the Nervous System of Vertebrates, Including Man, New York, The Macmillan Company, 1936. Beccari, N.: Neurologia comparata, Florence, Italy, Sansoni Edizioni Scientifiche, 1943.

6. Edinger, L.: Über die dem Oralsinne dienenden Apparate am Gehirn der Säuger, Deutsche Ztschr. Nervenh. **36**:151-160, 1908.

interpreted as the center of the "oral sense," shows a remarkably constant degree of differentiation in nonprimates,[7] as well as in primates,[8] in Tarsius or Galago,[9] as well as in man.[10] After all, even man enjoys his food. The reduction of the rhinencephalon is, however, a rather negative characteristic. To illustrate at least two positive "achievements" of the primates, let me show you in outline the hemispheres of a dog, of Tarsius, and of Galago [11] (Fig. 1). In the dog the outline of the lateral ventricle is roughly kidney-shaped. In Tarsius its outline is much the same, except for an unmistakable occipital horn; in Galago there is no occipital horn, but the posterior (or should I say, inferior?) horn shows a much sharper bend than in either dog or Tarsius. It has developed into a true temporal horn. These observations point to differences in cortical structures, fully borne out by cytoarchitecture. Tarsius has a very well-structured and very large striate, or visual, area, while the visual area of Galago differs but little from that of nonprimates, at least for its largest parts.[12] Solnitsky and Harman [13] observed, however, a beginning of the "primate" pattern in the central portion of the visual area of Galago, reminiscent of von Volkmann's [14] description of the visual area of the (arboreal) squirrel. Galago has well developed frontal and temporal lobes, as the

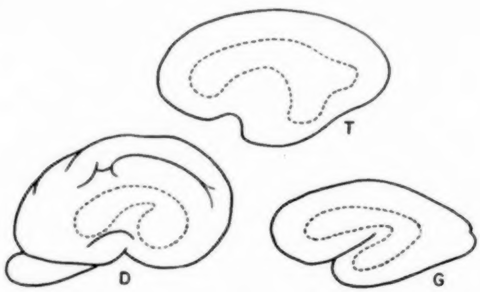

Fig. 1.—Cerebral hemispheres of dog, Tarsius, and Galago, showing lateral ventricles.

shape of its temporal horn suggests, while there is hardly a trace of a frontal or temporal lobe in Tarsius, which resembles in this respect the dog quite closely.

7. Fox, C. A.: Certain Basal Telencephalic Centers in the Cat, J. Comp. Neurol. **72**:1-62, 1940.

8. Lauer, E. W.: Nuclear Pattern and Fiber Connections of Certain Basal Telencephalic Centers in the Macaque, J. Comp. Neurol. **82**:215-246, 1945.

9. von Bonin, G.: The Isocortex of Tarsius, J. Comp. Neurol., to be published.

10. Crosby, C. E., and Humphrey, T.: Studies of the Vertebrate Telencephalon: II. Nuclear Pattern of the Anterior Olfactory Nucleus, Tuberculum Olfactorium and the Amygdaloid Complex in Adult Man, J. Comp. Neurol. **74**:309-352, 1941.

11. von Bonin, G.: The Cortex of Galago: Its Relation to the Pattern of the Primate Cortex, Illinois Monographs in the Medical Sciences, Vol. 5, No. 3, Urbana, Ill., University of Illinois Press, 1945.

12. von Bonin, G.: The Striate Area of Primates, J. Comp. Neurol. **77**:405-429, 1942.

13. Solnitsky, O., and Harman, P. J.: Regio Occipitalis of the Lorisiform Lemuroid Galago Demidovii, J. Comp. Neurol. **84**:339-384, 1946.

14. von Volkmann, R.: Vergleichende Cytoarchitektonik der Regio occipitalis kleiner Nager und ihre Beziehung zur Sehleistung, zugleich ein Beitrag zur Klärung von Bedeutung und Genese der Calcarinaspaltung, Arch. ges. Anat. (Abt. 1) **85**:561-657, 1928.

The evolutionist who tries to reconstruct the ancestral tree of man will have to note that neither Galago nor Tarsius possesses in its brain all features which distinguish primates from other mammals. The peculiar structure of the primate striate area and the large frontal lobe of the primates were, of course, known for a long time. What was not fully appreciated, but what the brain of Galago demonstrates clearly enough, was the parallelism in the development of the frontal and the temporal lobe. There may well be other distinguishing characteristics of the primate brains, but I shall not attempt to be exhaustive.

The functional parallel to these structural peculiarities of the primate brain which have just been described is not hard to find. The primates came to rely for the recognition of their environment on the sense of vision, rather than on that of smell, as most other mammals do. It is an attractive thought that this change was due to the arboreal life which the early primates must have led.[15] Efficient visual ability requires, of course, adaptation not only of the brain but of the eyes, and perhaps of other parts of the body as well. What we know [16] suggests that primates have eyes with a much greater power to accommodate than do lower mammals. This may be more important than the position of the eyes, which endows primates with binocular vision. For overlapping visual fields are not a *conditio sine qua non* for the perception of distance.[17] The beautiful architecture of the primate striate area may be more closely related to the ability of primates to see clearly objects rather near the eyes than to their binocular vision.

The development of the frontal and the temporal lobe is not quite so easy to interpret, since they apparently subserve functions which cannot readily be tested in the laboratory. The clinical observations of Penfield and his collaborators [18] may be cited. After extirpation of the frontal lobes, the patient is severely handicapped in planning ahead, and stimulation of the temporal lobe may lead to the rise into consciousness of past events or scenes.[19] Brought on a common formula, the fronto-temporal lobes have to do with the past and the future, with memory and forecasting. This, of course, is merely a rewording of observations made in the operating room and in the wards; it does not explain how it came about as an adaptation to the demands of environment.

It would appear that muscular abilities of primates differ profoundly from those of lower forms, not in the sense of more brawn, but in that of more brain. In lower mammals, and, a fortiori, in lower vertebrates, moving limbs form, with the external medium against which they are moved, "closed chains.[20]" In primates, many actions, such as the handling of small movable objects, reaching for an object, even jumping

15. Jones, F. W.: Arboreal Man, London, Edward Arnold & Co., 1916. Collins, E. T.: Arboreal Life and the Evolution of the Human Eye, Philadelphia, Lea & Febiger, 1922.

16. Martin-Oppenheim, S.: Metrische und descriptive Merkmale des menschlichen und tierischen Auges, Tabulae biol. period. **22**:54-153, 1947.

17. Gibson, J. J.: The Perception of the Visual World, Boston, Houghton Mifflin Company, 1950.

18. (*a*) Penfield, W., and Evans, J.: The Frontal Lobe in Man: A Clinical Study of Maximal Removals, Brain **58**:115-133, 1935. (*b*) Penfield, W.: Memory Mechanisms, A. M. A. Arch. Neurol. & Psychiat., this issue, p. 178.

19. This paragraph was changed after I had heard Dr. Penfield's presidential address.[18b]

20. von Baeyer, H.: Die Wirkung der Musklen auf die menschlichen Gliederketten in Theorie und Praxis, Ztschr. orthop. Chir. **46**:1-19, 1925. Rüssel, A.: Das Wesen der Bewegungskoordination, Arch. ges. Psychol. **112**:1-22, 1943.

to another branch among the trees of the jungle, are performed in "open chains." This requires a much finer control over the muscles and the "final common paths." Of course, the cat playing in its cruel way with a captured mouse, or the squirrel handling its precious nut, shows some ability to use "open chains," but this certainly cannot compare with the delicate skill of highest primates, e. g., the surgeon or musician. Speech, too, is essentially a use of "open chains." One can conceive of "progressive corticalization" as the correlate of this ability.

To get some idea of the trend of cerebral evolution among the primates, I have plotted weight of body and weight of brain on a double logarithmic scale. The graph (Fig. 2) shows remarkably little scatter. The slope of the regression line is steeper than it is among mammals in general.[21] In primates the weight of the brain

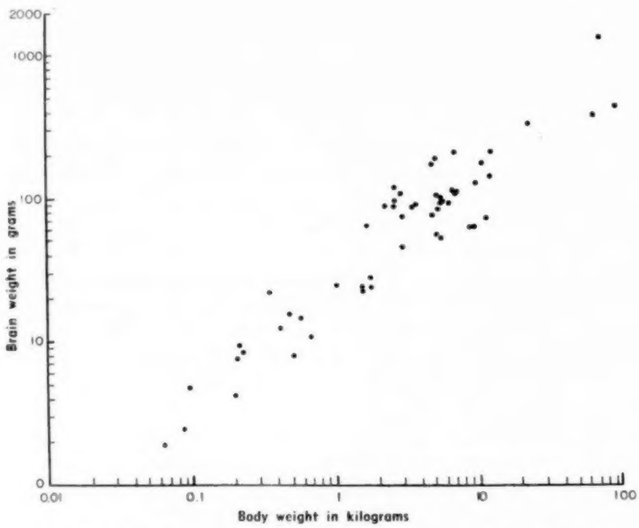

Fig. 2.—Brain weight in primates plotted against body weight on double logarithmic scale.

is proportional to the 0.75th power of the body weight, while in other mammals it is proportional to the 0.66th power. A theoretical interpretation of these figures is premature. The upper end of the "curve" in Figure 2 shows that man has about the brain weight that is coming to him by virtue of his size,[22] but that the anthropoid apes have a relatively small brain. The great discrepancy between the brain weight of man and that of the anthropoid apes is due to the disproportionally small brain of our nearest relatives rather than to the extraordinarily large brain of the human species.

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21. von Bonin, G.: Brain-Weight and Body-Weight of Mammals, J. Gen. Psychol. **16**:379-389, 1937.

22. Clark, W. E. L.: Deformation Patterns in the Cerebral Cortex, in Clark, W. E. L., and Medawar, P. B., Editors, Essays on Growth and Form, New York, Oxford University Press, 1945, pp. 1-22.

It is common knowledge that the "association areas" increase more than the sensory or motor areas as we go from smaller to larger brains among primates. Fortunately, we are able to observe these trends quantitatively, since the motor cortex is agranular and the sensory cortex is "koniocortex." While the latter statement, as we shall hear presently, has to be taken with a grain of salt, it is certainly true of the visual area. The next two graphs (Fig. 3*A* and *B*) plot again on a double logarithmic scale the size of the whole cortex against the size of the agranular precentral and that of the striate cortex. These graphs were prepared from data obtained by Dr. G. A. Shariff, who is now engaged in a quantitative study of some representative primate brains. Output, as indicated by the size of the agranular precentral cortex, varies much less than (visual) input. Moreover, the slope of the regression line is steeper for the precentral (output) than it is for the striate (input) area (35 degrees as against 25 degrees). The size of the associational cortex increases relative to that of the sensory cortex as one goes from small to large brains. The importance of this fact for theories of learning [23] is obvious.

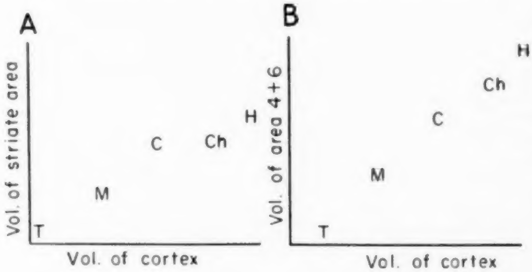

Fig. 3.—Volume of whole cortex plotted on double logarithmic scale against volume of (*A*) occipital koniocortex (visual) and (*B*) agranular precentral (motor) cortex.

But the problem of input is more complicated, for the histological recognition of somesthetic and acoustic areas is not possible, in spite of what has been said previously,[24] below the level of the macaque or the Cebus monkey. A renewed study of Hapale showed that in this little monkey the somesthetic area does not bear koniocortex. This is also true of Tarsius and Galago. Rose and Mountcastle's [25] recent studies on the thalamic somesthetic centers of the rabbit and cat, as well as Adrian's [26] observations on ungulates, make it clear that in lower mammals not much more than the face is represented on the cerebral surface. Whether the development of a true koniocortex goes hand-in-hand with the evolution of the somesthetic centers for the extremities is not yet established. Nor is it

23. Hebb, D. O.: The Organization of Behavior: A Neuropsychological Theory, New York, J. Wiley & Sons, Inc., 1949.

24. Peden, J. K., and von Bonin, G.: The Neocortex of Hapale, J. Comp. Neurol. **86**:37-63, 1947.

25. Rose, J. E., and Mountcastle, V. B.: The Thalamic Tactile Region in Rabbit and Cat, J. Comp. Neurol., to be published.

26. Adrian, E. D.: Afferent Areas in the Brain of Ungulates, Brain **66**:89-103, 1943.

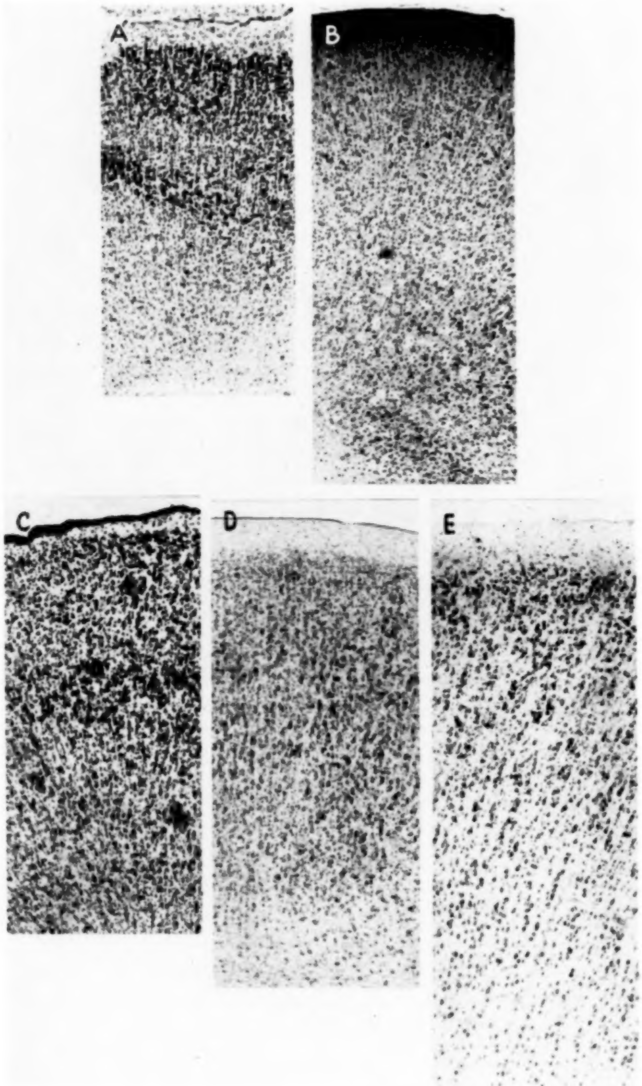

Fig. 4.—Histologic structure of inferior frontal gyrus (Broca's center) in (*A*) Galago, (*B*) Hapale, (*C*) Macaca, (*D*) chimpanzee, and (*E*) man.

clear whether the control of the muscles improves as the somesthetic areas develop. Does the use of "open chains" depend on a much finer "body scheme" than is present in the cortex of the rabbit or the pig?

To illustrate the trend of histological structure, we take as a first example the third frontal convolution, which in man's dominant hemisphere is known to all of us as Broca's convolution (Fig. 4). It is known since the days of Betz[27] that this part of the cortex shows particularly large cells in both the third and the fifth layer. A glance at the photograph will suffice to convince the reader that this feature is found in all five of the brains which have been sampled. There is little doubt, then, that we are dealing with homologous parts of the cortex; yet the differences between these animals are just as obvious as the similarities. The cell density diminishes from Galago to man, while the cell size appears to vary haphazardly. Ever since Nissl's[28] somewhat mystic discussion of his "nervous gray,"

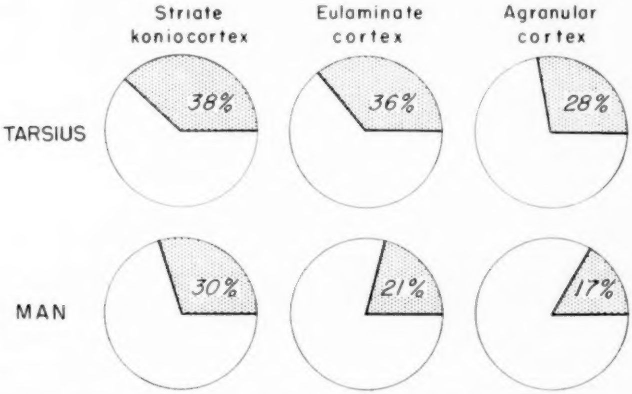

Fig. 5.—Cell-gray coefficients for three types of cortex in Tarsius and in man.

or neuropil, this concept has, in one way or another, influenced our thinking on the structure of the brain. Connections between neurons appeared to be located in this neuropil, and the number of these connections should, so it was argued, increase with the relative amount of "gray." von Economo[29] devised a numerical expression for the ratio of "gray matter" to cells and argued that it would constitute a measure for the degree of organization of a given brain. He determined it for the human brain (1:27), but for none other, so that his phylogenetic discussion remained in the realm of speculation. This was excusable, for the labor involved in its determination seemed at that time truly herculean. In the meantime, Chalkley[30] has

27. Betz, W.: Über die feinere Struktur der Grossehirnrinde des Menschen, Centralbl. med. Wissensch. **19**:193-195, 209-213, 231-234, 1881.

28. Nissl, F.: Nervenzellen und graue Substanz, München. med. Wchnschr., pp. 988-992, 1023-1029, 1060-1063, 1898.

29. von Economo, C.: Ein Koeffizient für die Organisationshöhe der Grosshirnrinde, Klin. Wchnschr. **5**:593-595, 1926.

30. Chalkley, H. W.: Method for Quantitative Morphologic Analysis of Tissue, J. Nat. Cancer Inst. **4**:47-53, 1943.

given us an excellent method which is reasonably fast. The cell-gray coefficient, i. e., the percentage of the total volume of the cortex occupied by cell bodies, becomes, indeed, progressively lower as one goes from Tarsius [31] to man. (This differs from von Economo's definition, used previously by me for the motor cortex.) Figure 5 shows graphically the cell-gray coefficient, as determined by the method of Chalkley for two primates.

Cell size is studied more easily, and therefore more accurately, by measuring the size of the nuclei than that of the cell bodies. As Bok [32] has shown, there is a simple arithmetical relation between the two. Let N be the volume of the nucleus, and C the volume of the cell; then we have $C = \frac{N^{2.01}}{90}$.

In the motor cortex, one can determine the mean volume of the nuclei of "ordinary" cells and that of the nuclei of "Betz" cells. The curves overlap slightly, and it is much more difficult to arrive at a satisfactory "cut" in the arm or face region than in the leg region, from which the figures cited here are taken. With these reservations, however, it is possible to compare the size of the two types of cells.[33] Their ratio changes quite considerably from smaller to larger brains, as the accompanying table shows. What this means in terms of function is still a mystery.

Average Nuclear Size, Expressed in Cubic Microns, in Area 4

	Giant Cells	All Others	Ratio
Galago	1,110	420	2.6
Cebus	1,131	306	3.7
Pan	2,450 *	484 *	5.1
Homo	2,328	371	6.3

* Arbitrary units.

We turn to corticocortical connections. Even without going into any details, it follows from the law of Baillarger and Dareste that the white matter increases less than the gray matter as the whole brain becomes larger. Hence, there is relatively more room for associational fibers in a lissencephalic brain than in a gyrencephalic one. What we know about the corticocortical connections of the macaque [34] and chimpanzee [35] from physiological neuronography appears to support this argument. As an example, Figure 6 shows the afferent connections to "Broca's area" in these two primates. Seven afferent paths are known in the macaque, but only four in the chimpanzee. Of course, negative evidence is no evidence. It may well be argued that the chimpanzee has simply been less thoroughly investigated than the macaque. Only because these findings confirm the general considerations just

31. von Bonin, G.: Cytoarchitecture of the Precentral Motor Cortex, in Bucy, P. C.: The Precentral Motor Cortex, Ed. 2, Urbana, Ill., University of Illinois Press, 1949, pp. 7-82.

32. Bok, S. T.: A Quadratic Relation Between the Volumes of the Nucleus and the Body of Ganglion Cells of Different Sizes, Psychiat. en neurol. bl. **38**:318-326, 1934.

33. von Bonin, G.: Studies of the Size of the Cells in the Cerebral Cortex: II. The Motor Area, J. Comp. Neurol. **69**:381-390, 1938.

34. von Bonin, G., and Bailey, P.: Neocortex of Macaca Mulatta, Illinois Monographs in the Medical Sciences, Vol. 5, No. 4, Urbana, Ill., University of Illinois Press, 1947.

35. Bailey, J.; von Bonin, G., and McCulloch, W. S.: The Isocortex of the Chimpanzee, Urbana, Ill., University of Illinois Press, 1950.

alluded to is one justified in attaching weight to them. Wiener [36] has pointed to the danger of "jamming" the available pathways which may threaten when the cortex becomes large and the connections do not increase proportionately. It may, perhaps with equal justification, be pointed out that too many connections may lead to mutual interferences, so that in the end nothing is left but a loud background noise. This may well be the situation in lower forms. Only when signals come in clearly, however, can they be reacted upon selectively. There may be an optimum of connections, and it may be that this optimum is established in the human brain. Is this, perhaps, the reason that the human brain has not only not increased, but actually somewhat decreased in bulk during the last 100,000 years or so? [37]

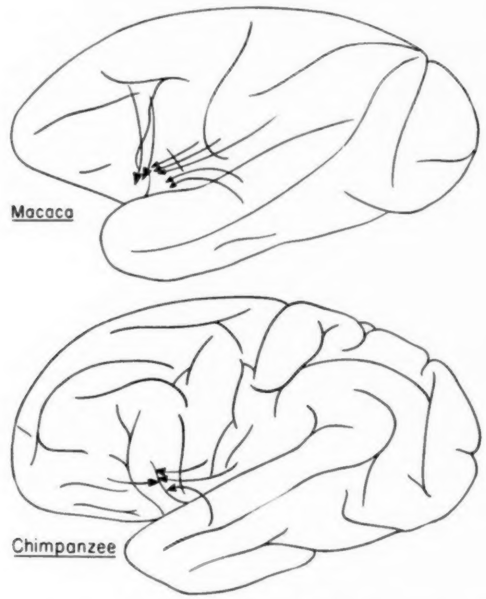

Fig. 6.—Corticocortical afferent connections to FCBm in Macaca and chimpanzee.

Under the influence of the Darwinistic school of comparative anatomy, Brodmann [38] had accepted it almost as an axiom that evolution meant progressive differentiation. His search for an ever-increasing number of cortical areas, definable by their architecture, seemed amply rewarded, although he himself admitted now and then that his subdivisions were "a little arbitrary." But when one looks with an unbiased eye at the cortex of man and, say, macaque, even Nissl preparations,

36. Wiener, N.: Cybernetics, or Control and Communication in the Animal and Machine, Cambridge, Mass, Technology Press, 1948.

37. von Bonin, G.: On the Size of Man's Brain, as Indicated by Skull Capacity, J. Comp. Neurol. **59**:1-28, 1934.

38. Brodmann, K.: Vergleichende Lokalisationslehre der Grosshirnrinde, in ihren Prinzipien dargestellt auf Grund des Zellenbaues, Leipzig, J. A. Barth, 1909.

studied assiduously for at least a half-century, can give one new insights. It is easily possible in the macaque to distinguish between frontal and parietal cortex. The former shows a "heaping up" of the large cells of the fifth layer against the lower border of the fourth layer, while the latter contains pyramidal cells in what is clearly layer *Vb*. This distinction is blurred in man. There is no way to distinguish easily and surely between frontal and (inferior) parietal cortex of the human brain. What impresses one most is the astounding homogeneity of the cerebral cortex of man.[39] It is easy to distinguish the three koniocortices, namely, the striate area and the postcentral (somesthetic) and supratemporal (acoustic) koniocortex, and one discerns next to each of these areas a parakoniocortex with large pyramidal cells in the lower reaches of the third layer. It is also easy to recognize the agranular varieties, namely, the gigantopyramidal and the simple precentral cortex, the anterior limbic and the posterior orbital cortex. All the rest is eulaminate cortex. Within this vast expanse, the superior parietal lobule stands out by virtue of its bipartite fourth layer; the inferior frontal convolution, by virtue of its large pyramidal cells in the third and the fifth layer, and the inferior temporal cortex, by virtue of its scanty third layer. All other distinctions described in the literature are tenuous, ill-defined and generally not clearly delimited. We gain perhaps more by thinking of the ability of these vast stretches of the cortex to function as a unit than to dwell on the concept of "elementary organs," as the classical school did. The individual cells within the eulaminate cortex are perhaps of no more significance than the individual molecules are in a mixture of gases.[40]

Much has been said about the similarity of brains to computing machines, and I have used on these pages such terms as "input" or "output," implying, so it would seem, acquiescence in such ideas. Let me suggest, in closing, that a computing machine can essentially only execute a program (although sometimes a very complicated one) that is given it by a human brain, but that the human brain appears to be able to program its own activity.

39. Bailey, P., and von Bonin, G.: Isocortex of Man, Illinois Monographs in the Medical Sciences, Vol. 6, No. 1-2, Urbana, Ill., University of Illinois Press, 1951.

40. Walter, W. G.: Functions of the Electrical Rhythms in the Brain, J. Ment. Sc. **96**:1-13, 1950.

AN ASCENDING RETICULAR ACTIVATING SYSTEM IN THE BRAIN STEM

H. W. MAGOUN, Ph.D.
LOS ANGELES

ONE ASPECT of the relation of the brain to the mind which may be contributed to by experimental study is concerned with the neural management of wakefulness. The waking state is certainly not essential to mental activity, for in the lighter stages of sleep vivid impressions may be experienced as dreams. In states of deep sleep, unconsciousness, or coma, however, mental activity seems practically in abeyance, and interrelations of the two have been expressed succinctly by Sherrington, in concluding a moving account of arousal from sleep, with the statement, "The brain is awakening and, with it, the mind returning."

The waking state has generally been thought to depend in an important fashion upon the arousing influence at the cerebral cortex of afferent messages initiated by sensory stimulation. It is a commonplace observation that afferent impulses from within or without can arouse a sleeping subject, and reduction of sensory impressions is routinely cultivated in seeking sleep. Bremer's [1] fundamental observation that after experimental transection of the mesencephalon, the reduced brain, lying *in situ* ahead of the cut, is in a state of sleep was thought to have its basis in the interruption of ascending sensory paths, and the conclusion from it, that sleep is due to deafferentation of the cerebrum, has been generally accepted.

Developments in electroencephalography have revealed pronounced differences in the electrical activity of the brain during wakefulness and sleep, which, being broadly similar in man and animals, have been utilized in recent laboratory investigations in the cat [2] and monkey.[3] If spontaneous electrical activity is recorded from

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From the Department of Anatomy, University of California School of Medicine at Los Angeles.

Read at the Seventy-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 18, 1951, as part of a symposium on the "Brain and the Mind."

This study was aided by grants to Northwestern University and to the University of California at Los Angeles from the Commonwealth Fund and the National Institute of Mental Health, United States Public Health Service.

1. Bremer, F.: Cerveau "isolé" et physiologie du sommeil, Compt. rend. Soc. biol. **118**:1235-1241, 1935.

2. (*a*) Jiminez-Castellanos, J.: Thalamus of Cat in Horsley-Clarke Coordinates, J. Comp. Neurol. **91**:307-330, 1949. (*b*) Lindsley, D. B.; Bowden, J. W., and Magoun, H. W.: Effect upon the EEG of Acute Injury to the Brain Stem Activating System, Electroencephalog. & Clin. Neurophysiol. **1**:475-486, 1949. (*c*) Lindsley, D. B.; Schreiner, L. H.; Knowles, W. B., and Magoun, H. W.: Behavioral and EEG Changes Following Chronic Brain Stem Lesions in the Cat, ibid. **2**:483-498, 1950. (*d*) Magoun, H. W.: Caudal and Cephalic Influences of the Brain Stem Reticular Formation, Physiol. Rev. **30**:459-474, 1950. (*e*) Moruzzi, G., and Magoun, H. W.: Brain Stem Reticular Formation and Activation of the EEG, Electroencephalog. & Clin. Neurophysiol. **1**:455-473, 1949. (*f*) Niemer, W. T., and Jiminez-Castellanos, J.: Cortico-Thalamic Connections in the Cat as Revealed by "Physiological Neuronography," J. Comp. Neurol.

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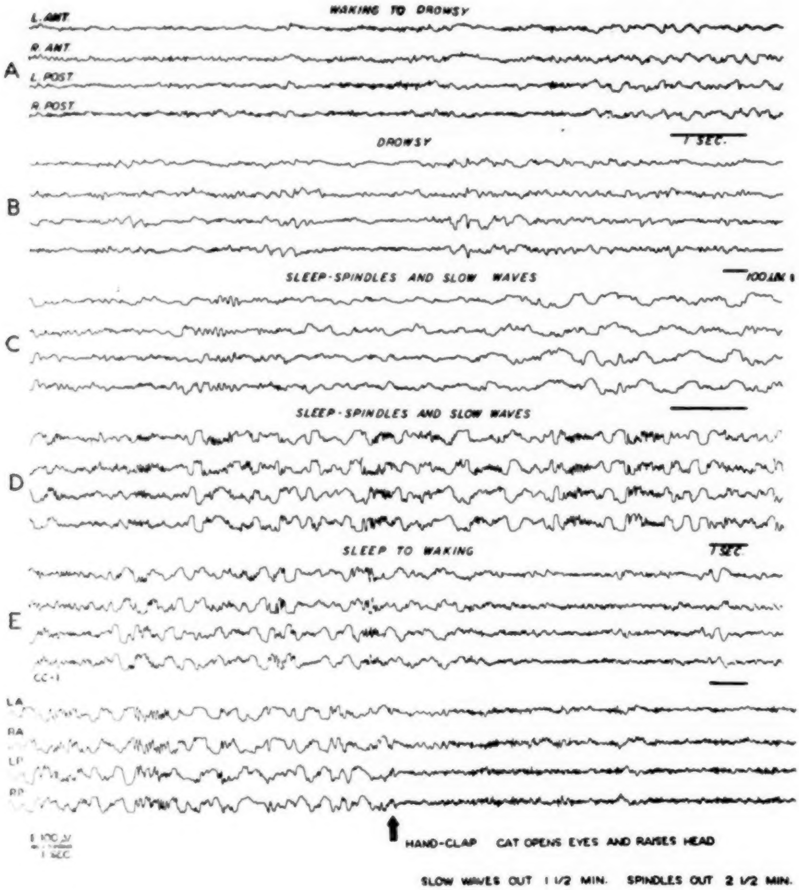

Fig. 1.—Upper (*A-E*), electrocorticogram of normal cat as it passed from wakefulness to sleep and reawakened (from Lindsley, Schreiner, Knowles, and Magoun [2c]).

Lower, electrocorticogram of sleeping cat awakened by handclap, at arrow (from Lindsley, Schreiner, Knowles, and Magoun [2c]).

93:101-123, 1950. (*g*) Rhines, R., and Magoun, H. W.: Brain Stem Facilitation of Cortical Motor Response, J. Neurophysiol. **9**:219-229, 1946. (*h*) Starzl, T. E., and Magoun, H. W.: Organization of the Diffuse Thalamic Projection System, ibid. **14**:133-146, 1951. (*i*) Starzl, T. E.; Taylor, C. W., and Magoun, H. W.: Ascending Conduction in the Reticular Activating System, with Special Reference to the Diencephalon, ibid. **14**:461-477, 1951; (*j*) Collateral Afferent Excitation of the Reticular Formation of the Brain Stem, ibid. **14**:479-496, 1951.

3. French, J. D.; von Amerongen, F., and Magoun, H. W.: Ascending Reticular Activating System in Brain Stem of Monkey, to be published. Starzl, T. E., and Whitlock, D. G.: Diffuse Thalamic Projection System in Monkey, J. Neurophysiol., to be published.

the cerebral hemispheres of a normal cat as it passes from wakefulness to sleep (Fig. 1, above), low voltage fast discharge, associated with alert wakefulness (*A*), is seen to give way to large slow waves and spindle bursts during sleep (*B-D*), while the alteration is reversed as the animal reawakens (*E*)—and the electroencephalogram is described as being desynchronized or synchronous in these contrasting states.

If the sleeping animal is awakened suddenly, as by a handclap, an activation pattern of low voltage fast discharge appears abruptly in association with behavioral alertness (Fig. 1, below). This alteration is termed the electrocorticographic arousal reaction, and it provides an objective record of the role of afferent stimulation in evoking the waking state, and of the characteristic maintenance of the arousal reaction beyond the period of the stimulus.

Present investigation of this subject began with the observation, seen in Figure 2, that direct electrical stimulation of a portion of the brain stem was capable of reproducing the electrocortical events encountered in awakening from sleep or in the electrocorticographic arousal reaction. The records in Figure 2 are from a cat under chloralosane (orthochloralose) anesthesia, in which the electrocorticogram somewhat resembles that of sleep in consisting of large slow waves. Brain stem stimulation, during the period marked by the heavy line, is seen to desynchronize the electrocorticogram in each record (*A-D*) and, when anesthesia is light (*A, B*), to induce low voltage fast discharge, simulating that observed in natural awakening or arousal.

An outline of the cat's brain (Fig. 10) shows the brain stem enlarging from the cord and overlaid by the cerebellum and cerebral cortex. The region whose direct stimulation desynchronizes the electrocorticogram is distributed through most of the length of the brain stem, in its central shaded core. Its rostral portion, in the midbrain and diencephalon, is most closely related to the cortex, and in a series of sections here (Fig. 3) shading marks the area whose direct stimulation desynchronizes the electrocorticogram.

Within it, two functional systems may be distinguished: The first can be identified as the laterally placed, ascending somatic and auditory paths, the direct stimulation of which, as far forward as the midbrain, sets up the arousing influence of peripheral excitation (Fig. 3, *H, G*). The second, from which the best effects are obtained, does not correspond in distribution to known anatomical paths and appears to be made up of a series of ascending relays coursing forward from the reticular formation of the lower brain stem, through the mesencephalic tegmentum, subthalamus and hypothalamus, and ventromedial thalamus, to the internal capsule (Fig. 3, *H-A*). The latter system is medially placed throughout, and the importance of its ascending influence, relative to that of afferent conduction, in maintaining the waking state has been evaluated by lesions placed, respectively, in the medial and lateral portions of the front of the midbrain.

A cat with mesencephalic interruption of afferent paths remains as wakeful as a normal animal and its electrocorticogram exhibits typical activation (Fig. 4*A*). In contrast, interruption of the ascending reticular activating system at the same level leaves the animal as though deeply asleep or anesthetized, and its electrocorticogram exhibits the large slow waves and spindle bursts of sleep (Fig. 4*B*). The lesion in this somnolent animal is seen in Figure 4*B* to have interrupted all ascending reticular relays to the forebrain, while sparing ascending sensory con-

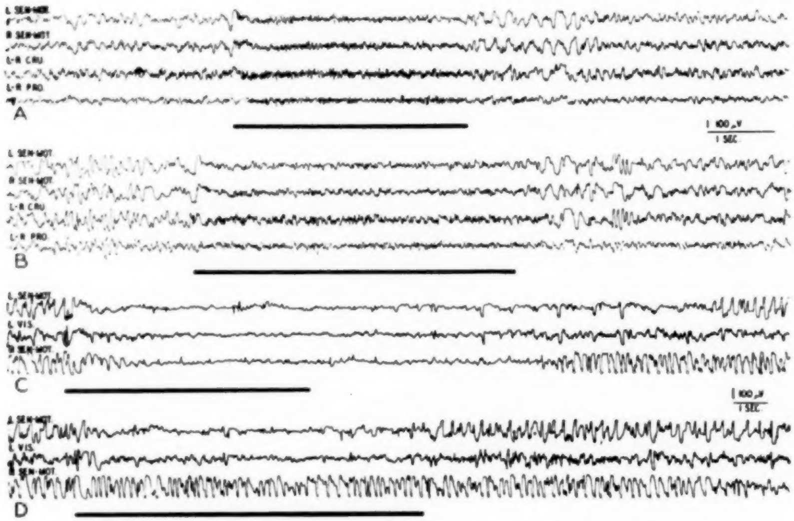

Fig. 2.—Effect of stimulation of reticular formation of brain stem upon electrocorticogram of cats under light (*A, B*) or deep (*C, D*) chloralosane anesthesia (from Moruzzi and Magoun [2e]).

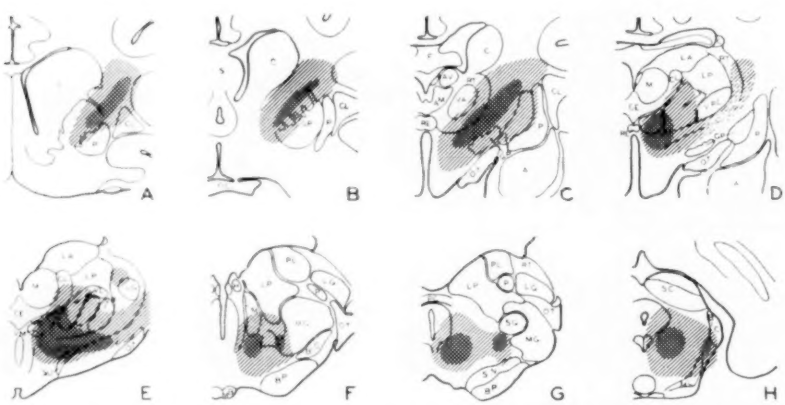

Fig. 3.—Transverse sections through right half of rostral portion of brain stem of cat, with shading marking areas whose direct stimulation desynchronized the electrocorticogram (from Starzl, Taylor, and Magoun [21]).

Abbreviations for all figures are as follows: *A*, aqueduct; *AM, AV*, anterior nucleus; *BIC*, brachium of inferior colliculus; *BP*, basis pedunculi; *C*, caudate nucleus; *CE, CL*, central nucleus; *CM*, centrum medianum; *F*, fornix; *GP*, globus pallidus; *H*, habenula; *LA, LP*, lateral nucleus; *LG*, lateral geniculate body; *M*, medial nucleus; *MB*, mamillary body; *MG*, medial geniculate body; *ML*, medial lemniscus; *NR*, red nucleus; *OC*, optic chiasm; *OT*, optic tract; *P*, putamen, pons; *PL*, pulvinar; *PRE*, pretectum; *RT*, reticular nucleus; *SC*, superior colliculus; *SN*, substantia nigra; *TEG*, tegmentum; *VA*, nucleus ventralis anterior; *VL*, nucleus ventralis lateralis; *VM*, nucleus ventralis medialis; *VP*, nucleus ventralis posterior.

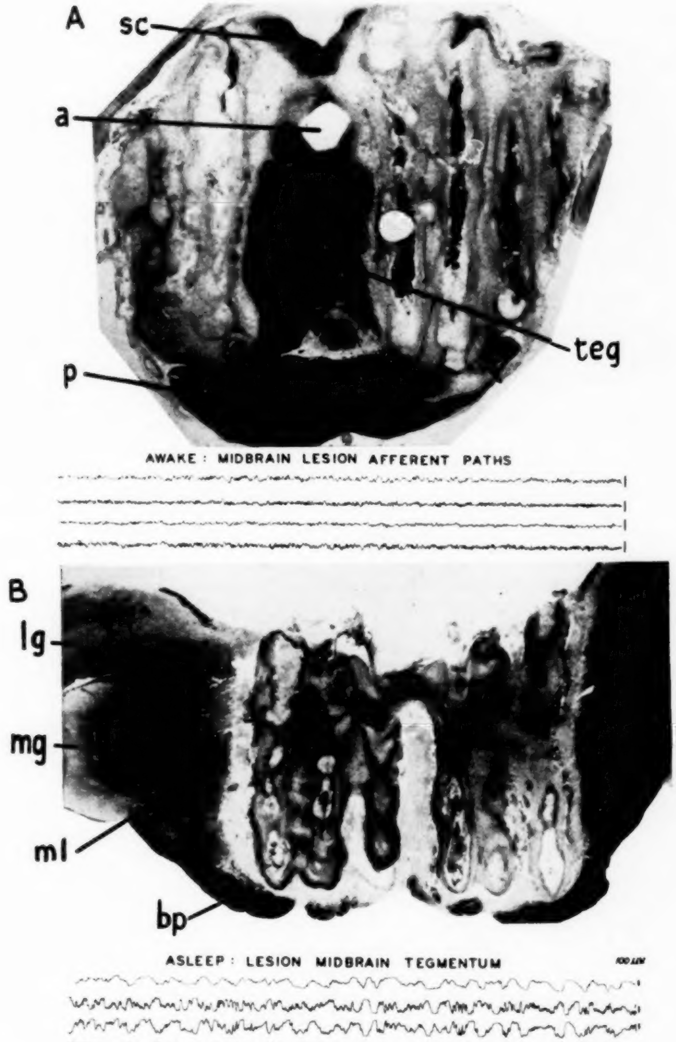

Fig. 4.—*A*, transverse section through rostral portion of midbrain, showing lesions interrupting auditory and somatic afferent paths bilaterally. A strip of waking electrocorticogram is included (from Lindsley, Schreiner, Knowles, and Magoun[2c]).

B, transverse section through rostral portion of midbrain, showing lesion of tegmentum, sparing lateral sensory and ventral motor paths. A strip of sleeping electrocorticogram is included (from Lindsley, Schreiner, Knowles, and Magoun[2c]).

nections to the cortex—somatic (*ML*), auditory (*MG*), and visual (*LG*)—and leaving long corticifugal or motor paths uninjured (*BP*).

The lesions in the waking animal (Fig. 4*A*) interrupt auditory and somatic afferent paths bilaterally and leave lower neural levels connected with the cerebrum only by the intact medial portion of the reticular formation (*TEG*). While such animals exhibit normal wakefulness, they can sleep as well, and when they are asleep both auditory and somatic stimulation are still capable of awakening the animal behaviorally and activating its electrocorticogram. Obviously, this can occur only by the ascending transmission of an activating influence through the

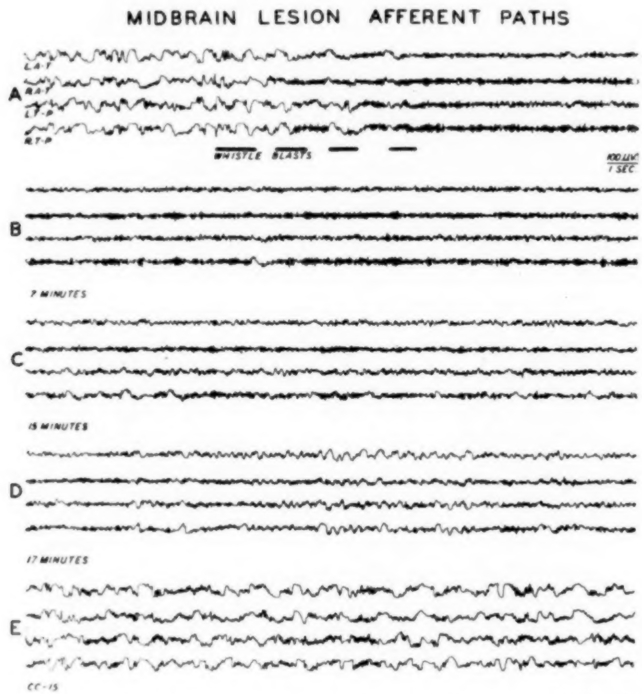

Fig. 5.—Electrocorticogram of cat with lesion seen in Figure 4*A*, showing arousal from sleep by whistle blasts, *A* (from Lindsley, Schreiner, Knowles, and Magoun [2c]).

medial reticular formation remaining, for the through sensory paths are blocked by the injury.

A record from the animal with the lesion seen in Figure 4*A* is shown in Figure 5. The cat starts out asleep and its electrocorticogram exhibits characteristic synchrony. Auditory stimuli, from a whistle, awaken the animal behaviorally and desynchronize its electrocorticogram (Fig. 5*A*), and some 15 minutes elapse before the cat returns to sleep (Fig. 5, *B-E*). Somatic stimuli have the same effect, and this arousal from sleep by excitatory stimuli, which the animal presumably cannot hear or feel, suggests that afferent stimuli induce or contribute to wakefulness not by the direct arrival of sensory discharge at the cortex, but

indirectly, and at a subcortical level, by excitation of the ascending reticular activating system within the brain stem. The characteristically prolonged duration of wakefulness beyond the period of the arousing stimulus may be suggested to depend upon maintained activity within interneuronal circuits, which the reticular formation possesses in such abundance.

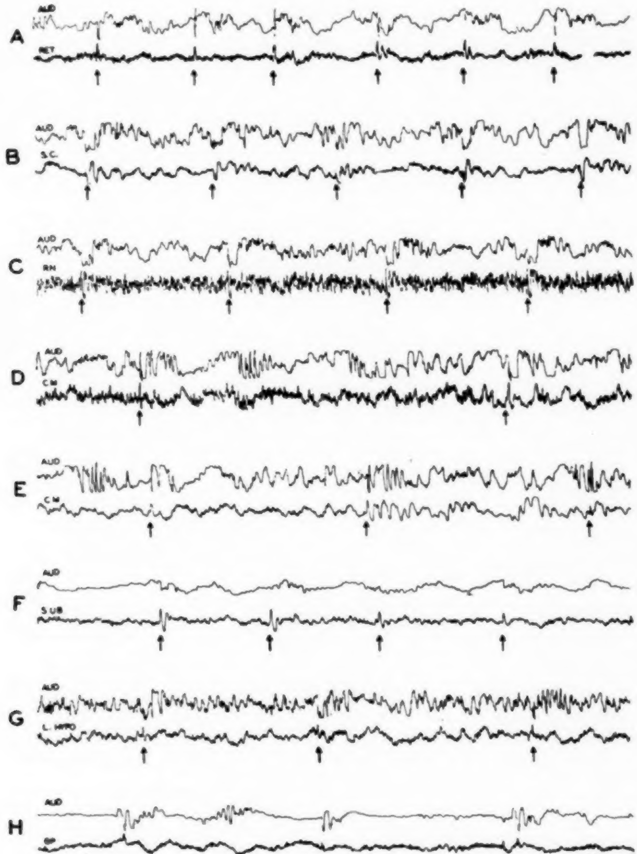

Fig. 6.—Records from auditory cortex (upper channel) and from (lower channel) midbrain tegmentum (*A*), superior colliculus (*B*), red nucleus (*C*), centrum medianum (*D*, *E*), subthalamus (*F*), hypothalamus (*G*), and globus pallidus (*H*). Click stimuli were delivered at arrows (from Starzl, Taylor, and Magoun [21]).

This postulated subcortical focus of arousal by afferent stimulation is supported by recent demonstration, in animals without central anesthesia, of a hitherto unsuspected wealth of afferent connections with the reticular activating system in the brain stem. In each of the strips in Figure 6, the upper channel records from the

auditory cortex and the lower channel variously from the medial reticular formation (*A*), the tegmentum (*C*), the subthalamus, (*F*) and the hypothalamus (*G*). Click stimuli were delivered at the arrows, and potentials are seen to be evoked regularly both in the auditory cortex and within the medial portion of the brain stem.

Shading, on the sections outlined in Figure 7, *A-F*, marks the area from which such evoked auditory potentials were recorded in the midbrain and diencephalon. The classic auditory path—the brachium of the inferior colliculus, the medial geniculate body, and the auditory radiation—is, of course, involved, but the medial reticular formation, the subthalamus and hypothalamus, and the ventromedial thalamus are implicated as well, and it is clear that auditory stimuli are firing the ascending reticular activating system.

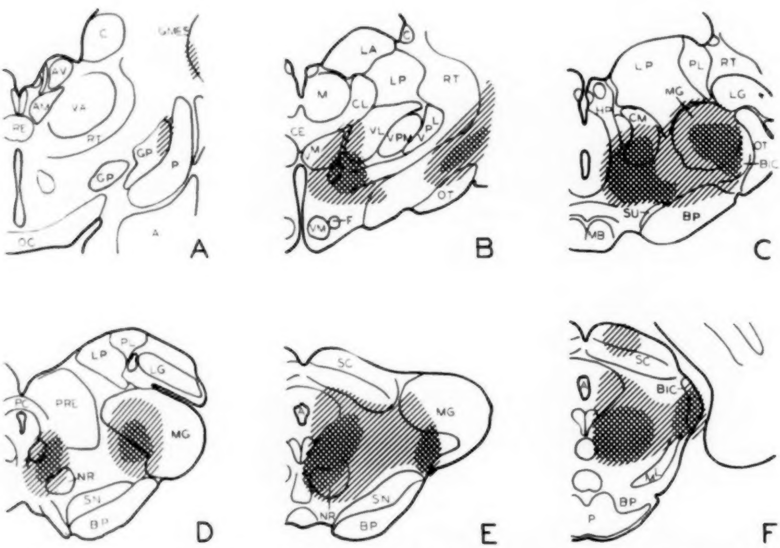

Fig. 7.—Transverse sections from rostral portion of brain stem of cat, with shading marking areas from which evoked potentials were recorded upon click stimulation (from Starzl, Taylor, and Magoun [23]).

The tracings shown in Figure 8 illustrate excitation of the reticular activating system by somatic afferent stimulation. In each strip, the upper channel records from the somatic receiving cortex, and the lower, from the medial thalamus or subthalamus. The six strips in Figure 8*A* show turnover of the potentials evoked by single shocks to the sciatic nerve (arrows) upon lowering the bipolar recording electrode by millimeter steps through the centrum medianum and the subthalamus. The four strips in Figure 8*B* illustrate the effect of repetitive sciatic stimulation (heavy line) upon the spontaneous electrical activity of the cortex and subthalamus. In records *1-4*, frequencies were 6, 15, 25, and 50/cps. Desynchronization of cortical electrical activity with high frequencies of sciatic stimulation is seen to be associated with discharge of the reticular activating system at 15/cps. or over.

Shading in Figure 9 *A* to *F* marks the area from which evoked potentials are recorded upon single-shock stimulation of the sciatic nerve. The through somatic pathway—the medial lemniscus and the nucleus ventralis posterior thalami—is clearly outlined, and again it is plain that the medial reticular formation, the subthalamus and hypothalamus, and the ventromedial thalamus are equivalently implicated. Such excitation of the ascending reticular activating system by afferent stimulation is still obtained after decerebellation or decortication and so does not depend upon conduction through cerebellar circuits or upon recurrent corticofugal discharge. It would appear, rather, to be effected by collaterals from afferent paths in the brain stem and propagation forward by reticular relays.

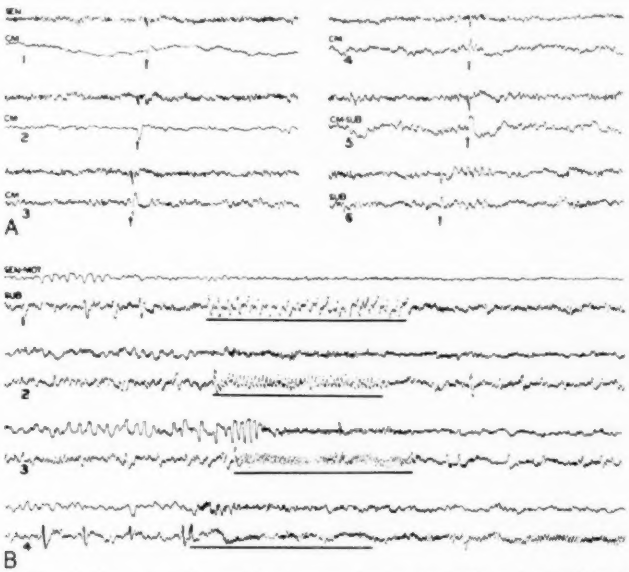

Fig. 8.—Records from somatic receiving cortex (upper channel) and medial thalamus and subthalamus (lower channel). In *A*, strips *1-6* show turnover of potentials evoked by single-shock stimuli to the sciatic nerve on lowering the bipolar recording electrode by millimeter steps through the centrum medianum and subthalamus (at the level of Figure *9D*).

In *B*, alterations in cortical and subthalamic electrical activity are seen (*1-4*) during repetitive stimulation of the sciatic nerve (heavy line) at 6, 15, 25, and 50 cps, respectively (from Starzl, Taylor and Magoun [23]).

Acknowledging, then, the demonstrable capacity of afferent stimuli to awaken a sleeping subject and the importance of diminution of afferent impulses in predisposing to sleep, recent investigation has identified an ascending reticular activating system in the brain stem (Fig. 10). Its direct stimulation reproduces the electrocortical events observed in natural awakening or arousal. Both old and recent observations have shown that injury to its rostral portion results in impairment of wakefulness. Into it passes such a wealth of afferent collaterals as to indicate that sensory involvement in the waking process is managed indirectly, and at a subcortical level, by modifying its activity.

As was earlier determined,[28] the same portion of the cephalic reticular formation of the brain stem when active exerts pronounced facilitatory influences upon lower motor outflows, and the possibility is apparent that it may normally

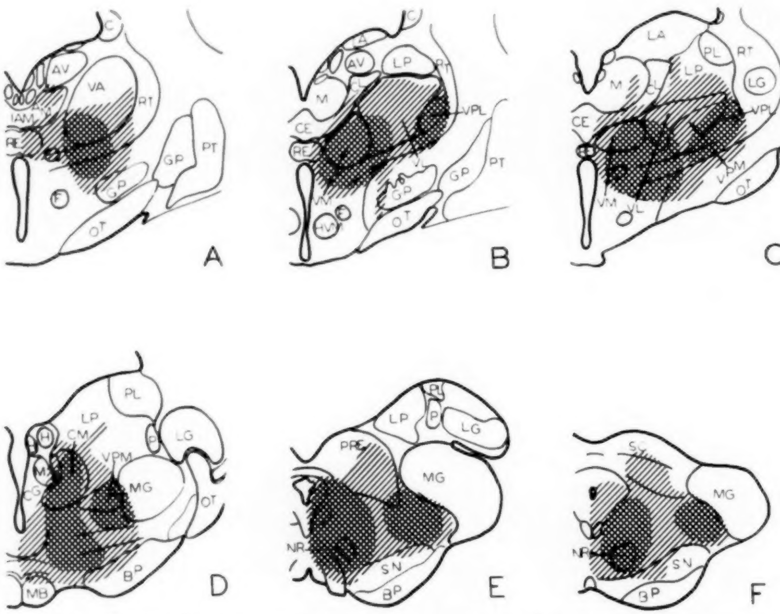

Fig. 9.—Transverse sections through the rostral portion of the brain stem of the cat, with shading marking the areas from which evoked potentials were recorded upon single-shock stimulation of the sciatic nerve (from Starzl, Taylor, and Magoun [23]).

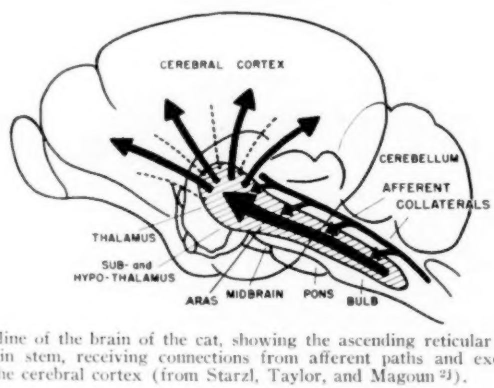

Fig. 10.—Outline of the brain of the cat, showing the ascending reticular activating system areas in the brain stem, receiving connections from afferent paths and exerting generalized influences upon the cerebral cortex (from Starzl, Taylor, and Magoun [23]).

function both in descending and in ascending directions—to subserve, on the one hand, the behavioral facility and, on the other, the central alertness that characterize the waking state.

CORTICOFUGAL PROJECTIONS TO THE BRAIN STEM

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COSIMO AJMONE-MARSAN, M.D.
AND
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IN THIS symposium, Professor Magoun has described some of the properties of the reticular system of the brain stem, with particular reference to mechanisms underlying alertness or arousal of the organism and its effect upon the electrical activity of the cortex. Emphasis has been placed upon that portion of this system lying in the basal part of the diencephalon and midbrain, with some extension into the mesial portion of the thalamus. From the results presented it would seem that the ascending portion of the reticular system in the more caudal part of the brain stem exerts its effect upon the electrical activity of the cortex in a generalized manner, without evidence of topographic localization.

In the thalamus there exists a more highly differentiated portion of this system, which we have tentatively described as the thalamic reticular system. Electrical stimulation within this system is capable of exerting a similar activating influence upon more restricted areas of the cortex, though activation of one portion may readily spread through a closely interconnected multineuronal network to all parts of it. Rapid local electrical stimulation causes a similar desynchronizing effect upon the electrical rhythms of the cortex, while slower repetitive stimulation (5 to 10 cycles per second [cps]) serves to time the electrical activity of the cortex, bringing the alpha-like rhythms under control of the thalamic stimulus. This effect was first described by Morison and Dempsey [1] as the "recruiting response" because of the increasing amplitude of response to the first few stimuli in a series when the frequency of the stimulus was nearly the same as that of the spontaneous rhythms. With careful exploration of the intralaminar and adjacent nuclei of the thalamus in the cat with minimal stimuli, we have regularly obtained clear recruiting responses from sensory receiving areas (somatic, visual, auditory, and olfactory), as well as from frontal and parietal association areas. These studies have also revealed a topographic organization within this system, in general, the mesial rostral portion projecting more prominently to the frontal regions, and the caudal and lateral portions to the posterior areas of the cortex. Stimulation in the vicinity of the nucleus reuniens has given the best responses from the uncus and the subcallosal

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From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

Read at the Seventy-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 18, 1951, as part of a Symposium on the Brain and the Mind.

1. Morison, R. S., and Dempsey, E. W.: A Study of Thalamo-Cortical Relations, Am. J. Physiol. **135**:281, 1942.

and orbital regions. Curiously, the occipital cortex has usually responded best to stimulation from the more rostral portion of the intralaminar region near the anteromedial nucleus. Further details of these studies, some of which have been carried out in collaboration with Droogleever-Fortuyn,[2] are to be reported elsewhere. They are summarized here, since they give a somewhat different picture of the thalamic reticular system than that recently reported by Starzl and Magoun.[3]

The synchronization, or timing, of cortical electrical activity is a feature of the thalamic reticular system which distinguishes it from the mesencephalic reticular system, from which no such timing of responses can be produced. However, in the presence of heightened desynchronizing effects from the mesencephalic arousal system, either due to local electrical stimulation or obtained in unanesthetized animals, recruiting and synchronizing effects cannot be set up by stimulation within the thalamic reticular system, the lower system apparently blocking the action of

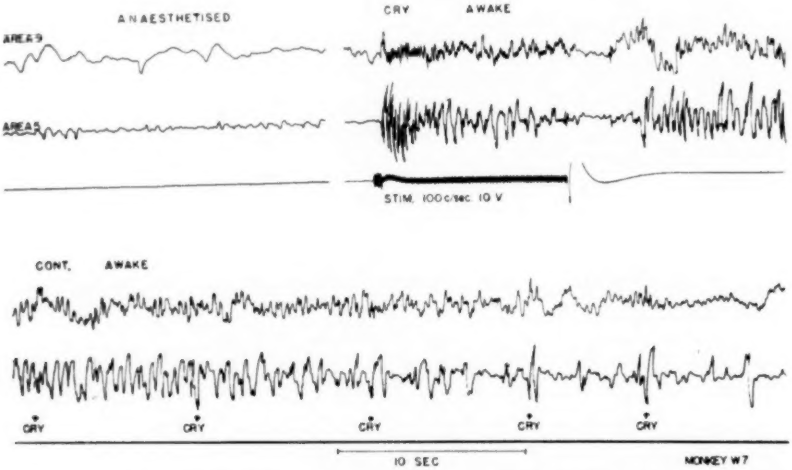

Fig. 1.—Electrocorticogram from frontal (Area 9) and parietal (Area 5) cortex in monkey described in text, showing effect of stimulating mesencephalic reticular formation adjacent to central gray matter at level of superior colliculus.

the thalamic system in its effect upon cortical rhythms (as shown originally by Moruzzi and Magoun[4] and confirmed by us).

The remarkable effectiveness of the mesencephalic reticular system in producing a generalized arousal of an animal is illustrated in the instance of a monkey anesthetized with pentobarbital sodium and suffering from depression of cerebral activity due to prolonged exposure of the brain and operative shock.

2. Jasper, H. H., and Droogleever-Fortuyn, J.: Experimental Studies on the Functional Anatomy of Petit Mal Epilepsy, A. Res. Nerv. & Ment. Dis., Proc. **26**:272, 1947. Jasper, H.: Symposium: Thalamocortical Relationships: Diffuse Projection Systems; The Integrative Action of the Thalamic Reticular System, Electroencephalog. & Clin. Neurophysiol. **1**:405, 1949.

3. Starzl, T. E., and Magoun, H. W.: Organization of the Diffuse Thalamic Projection System, J. Neurophysiol. **14**:133, 1951.

4. Moruzzi, G., and Magoun, H. W.: Brain Stem Reticular Formation and Activation of EEG, Electroencephalog. & Clin. Neurophysiol. **1**:455, 1949.

The electrocorticogram showed low voltage slow waves before stimulation, as seen in Figure 1. The animal was unresponsive to pain and exhibited no spontaneous movements. As soon as electrical stimulation (1-msec. pulses at 100 per second) was applied to a local portion of the mesencephalic reticular formation, adjacent to the central gray matter, he cried out, opened his eyes, struggled, and looked about, following objects with his eyes as though wide awake. The electrical activity of the cortex was suddenly changed to high voltage rapid discharges, as shown in Figure 1. The electrocortical activity of increased voltage continued for several minutes after the end of the mesencephalic stimulation; then the animal gradually became unresponsive again, and the electrical activity returned to its previously depressed state. The same process was repeated many times during the course of the experiment. The results show that the cortical arousal response need not be manifested by electrical activity of decreased voltage, but may be represented by an increase in voltage, if it is initially depressed.

A similar cry-and-arousal response of the animal in the foregoing experiment could be elicited by electrical stimulation of the anterior cingulate gyrus. This response suggested the possibility of a corticofugal projection from the anterior cingulate gyrus to the mesencephalic reticular formation. Consequently, we recorded the electrical activity from the same pair of

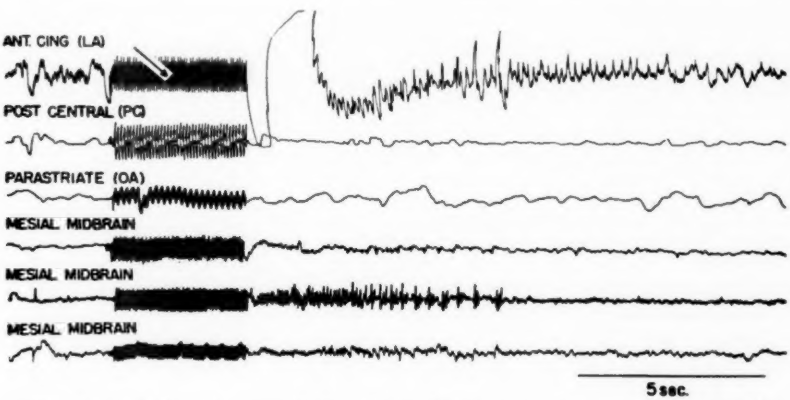

Fig. 2.—Activation of mesencephalic reticular formation—same site as that stimulated to produce arousal shown in Figure 1—by stimulation of anterior cingulate gyrus.

electrodes in the midbrain the stimulation of which had given rise to the arousal response during stimulation of the anterior cingulate gyrus. The rapid after-discharge was set up in the midbrain, as shown in Figure 2. A corticofugal projection to the reticular formation of the brain stem was demonstrated.

Observations on the arousal response in the human electroencephalogram has long suggested that this system in the brain stem not only must be controlled by the collaterals from the ascending afferent pathways, as described by Magoun, but must also have the patterns of cortical elaboration available to it. I shall cite only one example of many which could be brought to bear upon this problem, if time allowed.

A young woman, who was subject to narcolepsy, frequently dropped off into a deep sleep, from which she was very hard to arouse. The electroencephalogram showed the usual slow waves and spindles of normal sleep or the slower waves of deeper sleep. Pinching her or banging a bucket with a hammer near her ear failed to awaken her, though these stimuli produced some increase in electrical activity of the brain. Then her name was spoken softly, "Jean, Jean," and she immediately awakened, her electrocorticogram returning immediately to normal,

as shown in Figure 3. Many such examples of the perceptual discrimination of patterns of stimuli evoking an arousal response could be cited. It would seem that such processes must involve neuronal circuits of cortical elaboration.

To test this hypothesis, a series of experiments was carried out on monkeys. Local anesthesia and a quieting dose of pentobarbital sodium were used. The cortex was exposed widely and the head mounted in a stereotaxic instrument. A local electrical after-discharge was set up in an area of cortex by repetitive electrical stimulation. The intensity of the stimulus was adjusted to prevent spread of the after-discharge. It remained a local process, the discharges which were conducted to other areas over neuronal pathways being synchronized with the primary discharge and ceasing with the cessation of the primary discharge. Such conduction processes must be clearly distinguished from the spread of after-discharge which sets up autonomous paroxysmal discharges in areas other than that stimulated. This method of limited

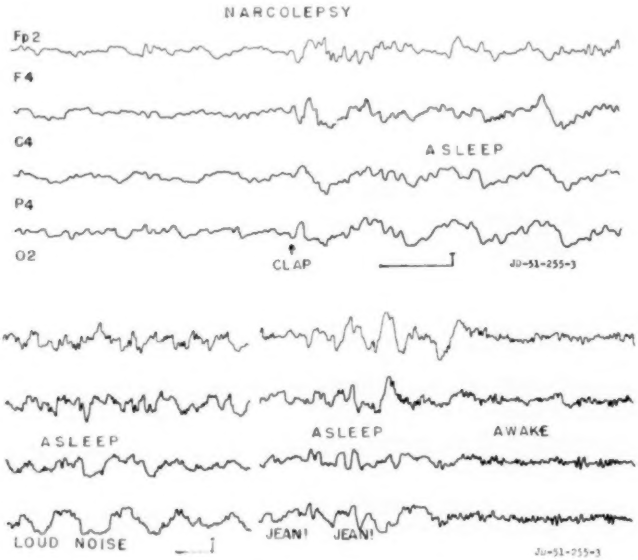

Fig. 3.—Electroencephalogram of narcoleptic patient described in text. Records are from an anteroposterior line of electrodes over right hemisphere, linked from frontal pole (*Fp2*) to occipital region (*O2*). Calibration line indicates one second and 50 microvolts.

local after-discharge makes it possible to study functional connections and corticofugal projection systems for local cortical epileptiform discharge. These discharges are not conducted antidromically. Usually direct nonsynaptic connections may be demonstrated when there is a one-to-one relationship between the primary and the conducted discharge, but the presence of strong synaptic relays is not ruled out by this method. The after-discharge method was previously used by Fields, King, and O'Leary [5] in studies of thalamocortical relationships.

Systematic exploration of the entire diencephalon and upper midbrain was carried out in order to map the subcortical projections of local cortical after-discharge from selected areas in the occipital, temporal, and frontal lobes. The diencephalon and midbrain were surveyed completely by recording electrodes placed 1 mm. apart on the frontal planes from 0 to + 13 mm. on the stereotaxic instrument. A total of over 2,000 local cortical after-discharges in nine

5. Fields, W. S.; King, R. B., and O'Leary, J. L.: Study of Multiplied Cortical Response to Repetitive Stimulation in Thalamus, J. Neurophysiol. **12**:117, 1949.

monkeys were required for these studies. Bipolar recording from serial pairs of electrodes made possible the localization of the maximum after-discharge to a subcortical area of about 1 mm. in diameter.

THE OCCIPITAL CORTEX

In the primary visual cortex (Area 17 of Brodmann, or *OC* of von Bonin) strong after-discharges could be set up without evidence of conduction to the parastriate area (Area 19 of Brodmann or *OA* of von Bonin). Even with very strong after-discharges set up in the primary visual cortex in over 400 trials in different animals, we were unable to detect conduction from the visual receiving area to the rest of the occipital cortex or to any other cortical area, thus confirming the results of Bonin, Garol, and McCulloch[6] with strychnine neuronography. Strong corticofugal projections were found, however, to a portion of the lateral geniculate body, and particularly to the lateral portion of the pulvinar in the thalamus, as shown in Figure 4. Some projection was also found to the region of the superior colliculus and the surrounding portion of the midbrain.

These results suggest that the preferential pathways of conduction from the visual receiving area of the cortex are not directly to other areas of the cortex, but

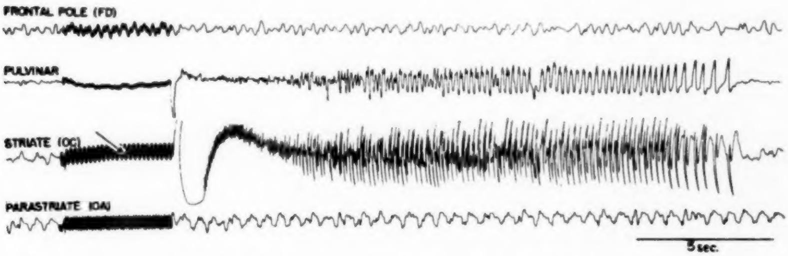

Fig. 4.—After-discharge from striate area (*OC*) conducted to pulvinar without conduction to parastriate area (*OA*) or to frontal pole (*FD*).

back to subcortical structures in the thalamus and midbrain. These are restricted local projections concentrated only in a narrow zone of the lateral geniculate body and adjacent portion of the pulvinar, and to a specific portion of the midbrain, with hundreds of other points throughout the diencephalon showing no trace of this after-discharge from the visual cortex, under the limiting conditions of our experiments.

After-discharges following stimulation of the parastriate area (*OA*) showed the same tendency to be conducted more readily to subcortical structures, as shown in Figure 5*A*. Irregular conduction into the adjacent parietal and temporal cortex did occur, as well as occasional conduction into the primary visual cortex (Fig. 5*B*) and rare weak conduction to the anterior frontal region. Corticofugal projections to the diencephalon and midbrain were found much more consistently than were the transcortical projections. They were also more widespread than were the projections from the primary visual cortex. The most important of these were to the pulvinar, to the intralaminar nuclei of the thalamus, to the mesencephalic reticular formation, and to the substantia nigra and subthalamic region.

6. von Bonin, G.; Garol, H. W., and McCulloch, W. S.: The Functional Organization of the Occipital Lobe, Biol. Symposia **7**:165, 1942.

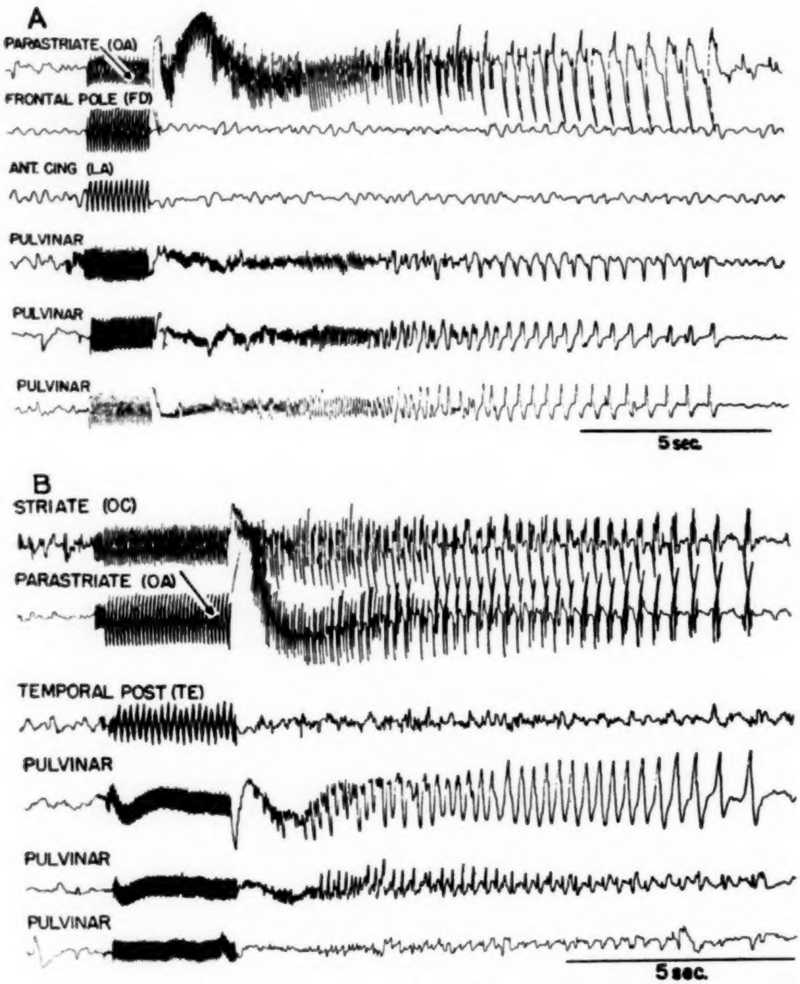

Fig. 5.—*A*, after-discharge following stimulation of parastriate area (*OA*) conducted to several points in pulvinar without conduction to other cortical areas. *B*, after-discharge following stimulation of parastriate area in another experiment, showing conduction to pulvinar and to striate cortex (*OC*) without conduction to posterior temporal region (*TE*).

A summary of the points of definite projection of after-discharge from the occipital lobe, as reconstructed from histological controls of the site of recording electrodes, is charted on cross-sectional diagrams in Figure 6. The relative predominance of points from the parastriate area (rectangles) as compared with those from the striate visual cortex (triangles) is striking. The overlapping of projections in the lateral portion of the pulvinar suggests that corticothalamocortical circuits may be more important than transcortical circuits in the relation of these two portions of the visual system. The absence of projections from the striate cortex directly to the intralaminar regions of the thalamus, with rich projections from the parastriate cortex, is also important, as will be discussed later.

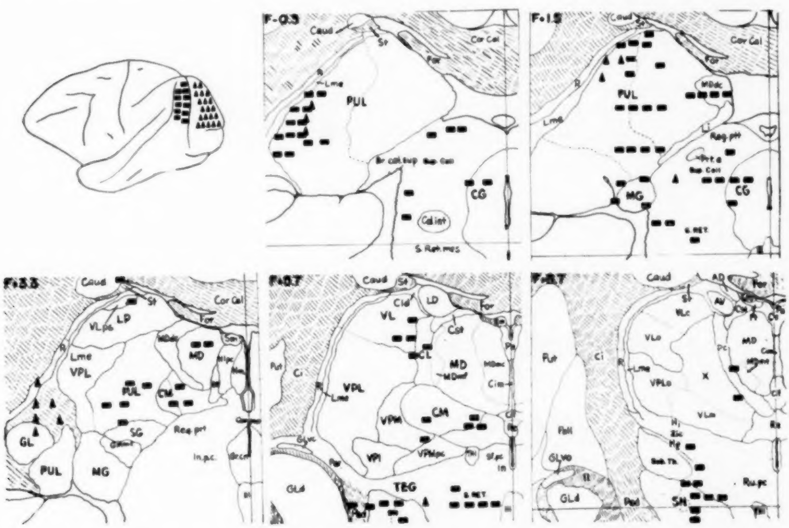

Fig. 6.—Summary of subcortical points from which after-discharge was conducted after stimulation of striate (triangles) and parastriate (rectangles) occipital cortex.

Diagrams of the diencephalon of the monkey (Macaca malatta) are from an atlas, soon to be published, prepared by Dr. Jerzy Olszewski. Frontal planes of stereotaxic coordinates are shown in the upper left-hand corner of each chart. All points were plotted from histological controls of serial frozen sections, after positions of recording needles had been marked by electrolytic deposit of iron at critical points and staining with ferrocyanide. Histological structure, and not coordinate measurements, were used in these plots, as the latter were found to be unreliable. Abbreviations used in these, and in succeeding, charts are as follows: *PUL* pulvinar; *sup. coll.*, superior colliculus; *CG*, central gray matter; *MD*, nucleus medialis dorsalis; *GL*, nucleus geniculatus lateralis; *GM*, geniculatus medialis; *VPL*, nucleus ventralis posterolateralis; *CM*, centrum medianum; *CL*, nucleus centralis lateralis; *SG*, nucleus suprageniculatus; *SN*, substantia nigra; *Zic*, zona incerta; *Sub. Th.*, nucleus subthalamicus; *S. Ret.*, substantia reticularis; *TEG*, tegmentum; *VL*, nucleus ventralis lateralis; *LP*, nucleus lateralis posterior; *VA*, nucleus ventralis anterior; *AM*, nucleus anteromedialis.

THE TEMPORAL LOBE

Four local areas of the temporal region were studied: the tip (*TG*), the anterior portion of the first temporal convolution (*TA*), the insula, and the posterior portion of the temporal region (*TE*). After-discharges from the anterior temporal region and the insula were readily conducted to the anterior frontal and

cingulate cortex, but the corticofugal projections from the temporal region did not depend upon these transcortical connections. The principal subcortical projections were to the pulvinar and lateralis posterior complex of the thalamus and to a portion of the medial geniculate and suprageniculate regions, with some to the intralaminar nuclei of the thalamus (except for the tip and the first temporal convolution). There were also projections to the substantia nigra and to the mesencephalic reticular formation. Particularly strong after-discharges were recorded from the mesencephalic reticular formation, as shown in Figure 7, after stimulation of the tip of the temporal lobe. We have presented elsewhere further details concerning the subcortical connections of the tip of the temporal lobe in the cat and the monkey,

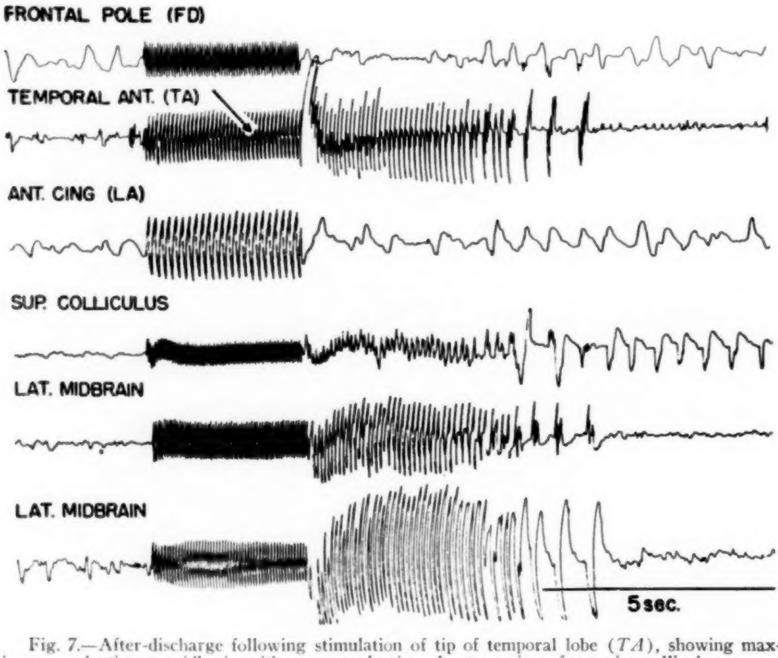

Fig. 7.—After-discharge following stimulation of tip of temporal lobe (*TA*), showing maximum conduction to midbrain with some conduction also to region of superior colliculus.

as determined by more complete electrographic study with strychnine neuronography and single-pulse stimulation, in addition to the after-discharge method.[7]

A summary of the subcortical projections of after-discharge from three separate areas in the temporal region, in addition to studies on the insular cortex, is presented in cross-sectional diagrams in Figure 8. Projections from the posterior temporal region (Area 37 of Brodmann, shown by triangles) were always found to be particularly strong, numerous, and widespread. It is to be noted that projec-

7. Stoll, J.; Ajmone-Marsan, C., and Jasper, H. H.: Electrophysiological Studies of Subcortical Connections of Anterior Temporal Region in Cat, J. Neurophysiol. **14**:305, 1951. Ajmone Marsan, C., and Stoll, J., Jr.: Subcortical Connections of the Temporal Pole in Relation to Temporal Lobe Seizures, Arch. Neurol. & Psychiat. **66**:669 (Dec.) 1951.

tions to the centrum medianum were found from the posterior temporal cortex and from the insula, though not from the tip of the temporal lobe. This observation has been confirmed in the more extensive studies,[7] mentioned above. In addition to the obviously important projections to the pulvinar, the concentration of projections in the region of the magnocellular portion of the medial geniculate body and in the nucleus suprageniculatus is of particular interest. It is from the latter region that recruiting responses can be most readily set up in the temporal lobe on local thalamic stimulation, suggesting that the nucleus suprageniculatus may be considered a portion of the thalamic reticular system, broadly defined.

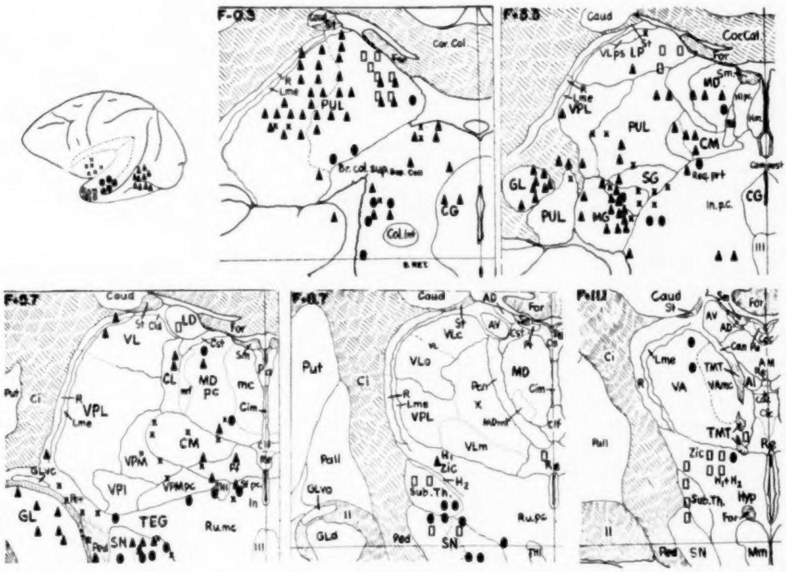

Fig. 8.—Summary charts showing in cross-sectional diagrams points to which after-discharge was conducted from three parts of temporal lobe and from insula.

THE FRONTAL REGION

We have studied two portions of the frontal region—the frontal pole (*FD* of von Bonin) and the anterior cingulate gyrus (*LA*). These two regions seemed to have close functional interconnections, as judged by the facility with which after-discharges were conducted from one to the other in either direction. Corticofugal projections showed some overlap, but several regions to which the frontal pole projected received no projections from the anterior cingulate gyrus. The strongest projections were to the intralaminar nuclei of the thalamus and adjacent portions of the nucleus medialis dorsalis and nucleus ventralis anterior, with important projections also to the subthalamus, the hypothalamus, and the midbrain. The conducted after-discharges in the principal intralaminar nucleus, centrum medianum, were particularly strong from the frontal and anterior cingulate regions, as shown in Figure 9*A*. A self-sustained after-discharge set up in the centrum medianum

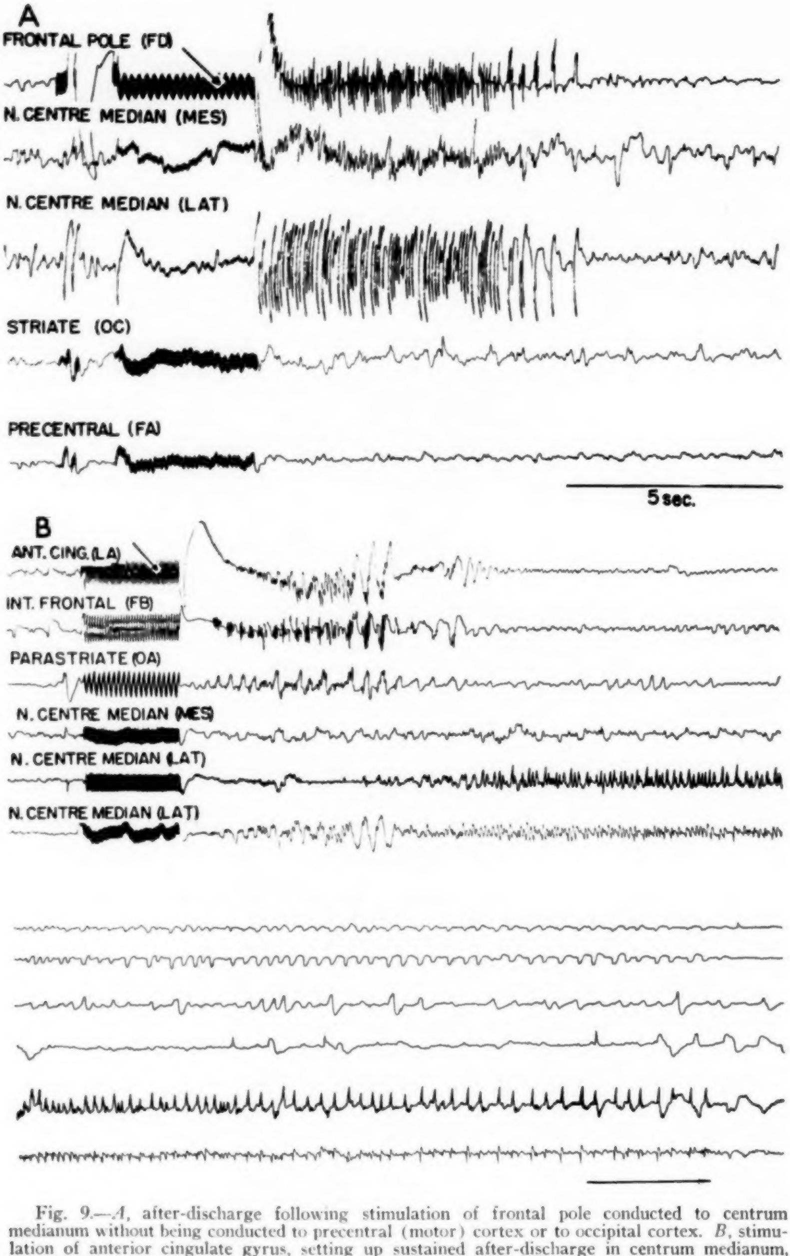

Fig. 9.—*A*, after-discharge following stimulation of frontal pole conducted to centrum medianum without being conducted to precentral (motor) cortex or to occipital cortex. *B*, stimulation of anterior cingulate gyrus, setting up sustained after-discharge in centrum medianum, which continued for 42 seconds after end of after-discharge in anterior cingulate gyrus. Note that spikes from the centrum medianum tend to fire back into anterior cingulate gyrus in second strip of record, which is continuation of first. Line at end indicates five seconds.

after a brief after-discharge in the anterior cingulate region is shown in Figure 9*B*. This is one of the rare subcortical self-sustained after-discharges set up by cortical stimulation in this series of experiments.

A reconstruction of the projection points from the frontal pole (triangles) and anterior cingulate gyrus (ovals) is presented in cross-sectional diagrams in Figure

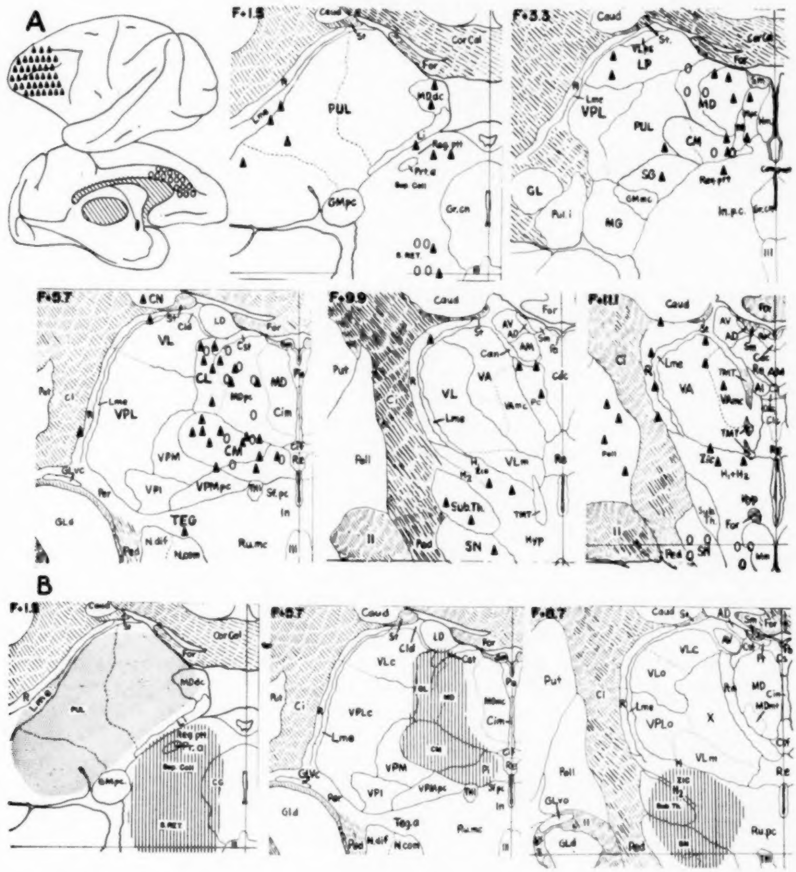

Fig. 10.—*A*, chart of points from which after-discharge was conducted after stimulation of frontal pole (triangles) and of anterior cingulate gyrus (ovals). *B*, chart of regions of maximum overlap of corticofugal projections shown in detail in previous figures. The three areas of vertical hatching indicate zones of maximum overlap from all areas studied, with exception of visual receiving area (*OC*), which did not project to thalamic area of overlap shown in second chart (*F* 5.7). Dotted zone in pulvinar indicates projection areas from temporo-parieto-occipital cortex.

10*A*. Projections from the frontal pole to intralaminar nuclei (centrum medianum paracentrale and nucleus centralis lateralis) were consistently more numerous and

stronger than those to portions of the nucleus medialis dorsalis. Projections to these same areas from the anterior cingulate gyrus were found, though no projection from the anterior cingulate to the nucleus anteromedialis were determined.

OVERLAPPING AREAS OF PROJECTION

When presenting the results of corticofugal projections from the occipital, temporal, and frontal regions, we noted that areas in the thalamus, basal diencephalon, and midbrain received projections from all cortical areas studied, with the exception of the primary visual receiving area. There seemed to be three principal zones of overlapping projection: (*a*) the reticular formation and tegmentum of the midbrain; (*b*) the intralaminar nuclei of the thalamus, with adjacent portions of the nucleus ventralis anterior and nucleus medialis dorsalis, rostrally, and adjacent portions of the pulvinar and nucleus suprageniculatus, caudally, and (*c*) the subthalamic region, including the subthalamic nucleus and substantia nigra, as shown in Figure 10*B*. The pulvinar and lateral nuclear complex of the thalamus were chiefly a common overlapping projection area from the temporal, parietal, and occipital cortex. It is clear that those areas of the diencephalon and midbrain stimulation of which produced generalized regulatory effects upon the electrical activity of wide areas of cortex also received projections from many cortical areas. This seems to lend experimental confirmation to the hypothesis that there exists a network of closely interconnected neurones in the upper brain stem (including the thalamus) which receive impulses from widespread cortical areas. This central reticular formation might, therefore, serve an over-all integrative function for many specific cortical activities of the frontal, temporal, parietal, and occipital lobes, for here, within a few millimeters, one finds interconnected groups of neurones, with ascending projections to widespread areas of cortex and corticofugal projections back into the same system.

These experimental findings may offer additional evidence for a centrencephalic integrating mechanism, to be discussed by Dr. Penfield in another communication. In this system of the brain stem there seem to be different portions or levels. The pulvinar and lateralis posterior complex of the thalamus would seem to be capable of correlating signals from the temporoparieto-occipital cortex. This may be a "mixing network," in which memory images are formed from information received over various sensory channels. It would seem, however, that this information is not directly projected into the centrencephalic system but must pass first through its own sensory elaborative system, since the primary receiving areas themselves, such as the striate visual cortex, do not project into the common regions of overlap, as does the parastriate area. (In preliminary experiments, this would seem to be true also for the primary somatic sensory receiving areas.)

Speculation regarding the significance of the thalamic, subthalamic, and mesencephalic portions or levels of overlapping projection is premature, but the effects of local direct stimulation in these regions of the brain stem give evidence of suggestive value. As a working hypothesis, we would propose that the projections into the thalamic reticular system may be related to mechanisms of attention, projections to the subthalamic region may have to do particularly with motor integrations, and projections to the mesencephalic reticular formation may bring the arousal mechanisms described by Professor Magoun into direct relation with impulses from widespread areas of the cerebral cortex.

DISCUSSION ON PAPERS BY DRS. VON BONIN, MAGOUN, AND JASPER AND ASSOCIATES

Dr. Henry Alsop Riley, New York: In the preparation of this discussion, I was somewhat hampered by the fact that I received a copy of only one paper, that by Dr. Jasper and his associates, so that I had to depend for my information upon the program abstracts of the papers by Dr. von Bonin and Dr. Magoun.

In reading the abstract of Dr. von Bonin's paper, I found it so short and categorical that I was unable to pick out any particular points for my discussion. I have not sufficient acquaintance with the technicalities suggested by Dr. Magoun's abstract, and I shall leave the real discussion of his paper to those more versed in neural physiology, namely, Dr. Bard and Dr. O'Leary.

I wish to draw attention to the brain-stem activities which have been recognized only recently and which suggest a much more extensive and comprehensive function for the reticular formation. It is of extreme interest and significance that this region of the brain stem is now being viewed as providing activities which are related to some of the highest organizations of the central nervous system, such as electroencephalographic patterns, wakefulness, and lethargy, and also with descending controls which express themselves through autonomic activities, although it would seem self-evident that states of varying wakefulness or lethargy would be integrated with autonomic activities governing the internal milieu.

With regard to Dr. Jasper's paper, I am somewhat confused by his reference to the diencephalic reticular substance. So far as I am aware, there has been no exact delimitation of this mass of gray matter. The structures of the mesencephalic tegmentum as they are followed upward become compressed into the area tegmentalis, the field of Forel, representing the fiber masses of the tegmentum. The zona incerta and the substantia innominata are the rostral continuations of the gray reticular formation. Field H 1 is mainly concerned with rostral projections, and Field H 2, with descending connections. A nucleus in the diencephalon called the reticular nucleus is situated in the lateral limiting medullary lamina of the diencephalon, and its structure suggests that it is not true reticular substance, but only a part of the lateral thalamic nucleus. Without specifically mentioning the diencephalic reticular structures, Dr. Jasper has referred to the nucleus reuniens; the intralaminar nuclei; the adjacent portions of the nucleus ventralis, pars anterior; the nucleus dorsalis; the pulvinar; the suprageniculate region; the subthalamus, and the substantia nigra.

The suggestions of Dr. Magoun and Dr. Jasper and their co-workers that the lower brain-stem levels exercise an important influence over the conditions of awareness and responsiveness are fascinating and open up great fields for further investigation by means of methods which have not hitherto been available. Those who have previously labored to identify fiber tracts connecting higher and lower centers have had no means of determining the direction of impulses carried by the fibers of these tracts, and knowledge of the nature of these tracts and nuclei has been based upon staining reactions and the unreliable alterations dependent upon ascending and descending degenerations. The newer electrical methods provide investigational techniques which are infinitely more exact and dependable.

The data at hand are still limited in extent, and the concept of the mechanisms by means of which these higher-to-lower relations, and vice versa, are provided is still subject to further conjecture and speculation. The reciprocal relations of the activities of the diencephalic and mesencephalic reticular formations are unclear as to their significance and require further elucidation. The apparent correspondence of the effects of stimulation of the ascending reticular system and the rostral portion of the cingulate gyrus provides further confirmation of the belief that the greater part of the limbic lobe has nothing to do with olfaction, but is endowed with much more highly integrated cortical activities.

The detailed data in regard to projections from various cortical areas to the diencephalon and mesencephalon, and vice versa, are still incomplete and do not seem to add up to any definitely understandable functional mechanisms. It is difficult to understand the absence of direct projections from the striate to the parastriate regions, the latter always having been considered the area of association and integration of the visual function. It is particularly difficult to understand the necessity for projections from the striate areas to the geniculate and the pulvinar, collicular, and mesencephalic levels and a return projection to the occipital region.

It is evident from these investigations that many of our simple, and perhaps quite naïve, conceptions of the activities of many cellular collections and fibrous structures are due for drastic and thorough revision. These electrical methods of investigation are infinitely more delicate than the crude anatomical and experimental procedures upon which many of our present conceptions are based. There still remains the difficulty of transferring data obtained by investigations on animals to human problems. The electrical methods of investigation have overturned many of our older concepts of the functions of various gray masses and fibers. The direction of discharges from the substantia nigra over the central tegmental tract and the area lenticularis, to pick only a few, may in time receive acceptable confirmation.

The reticular formation of the brain stem has been studied extensively by cytological and fiber-staining techniques. The functions of the cerebral nuclei have been rather well elucidated, but, exclusive of these structures, the reticular formation of the brain stem constitutes three-fifths of the mass of the brain stem. Collections of similar-appearing cells have been found in various parts of the reticular formation, but no adequate conception of the functional significance of these nuclei has been postulated.

Recently the circuits of many brain-stem mechanisms have been attributed to the reticular formation, but there still remain potentialities in the reticular formation whose elucidation may contribute greatly to our understanding of the physiology of the central nervous system. The only identified descending reticulospinal projections constitute the medial and lateral reticulospinal tracts, but great masses of fibers enter the circumgriseal ground bundles and may contribute other extensive descending reticular connections. Similarly, much more can be learned of the ascending reticular connections. These additions to our knowledge would aid materially in the understanding of many present-day problems.

We are at the threshold of great advances in our knowledge of the activities of the central nervous system. In the fragmentary and disconnected form in which our knowledge of these activities is represented, it is extremely difficult to envision the inner significance of much of these data. With further investigation, a comprehensible scheme will undoubtedly be disclosed. The older methods of investigation have probably yielded almost their maximum of information, and we shall have to depend upon these newer methods for further delving into Pandora's box.

Too much praise cannot be given to those who are now engaged in these fruitful and promising studies.

Dr. Percival Bailey, Chicago: I have not had the opportunity to read any of these papers, but I have been very interested in listening to them. I differ somewhat in opinion from my colleague and friend, Dr. Gerhardt von Bonin. There is no difference as to facts, but only as to opinions. Our collaboration is almost as vocal, as our friends know, as the family controversy that went on in the hotel room next to mine last night.

In my opinion, we have not made an adequate search for afferent impulses to FOBM in the chimpanzee. I think it is premature to say that there are fewer than there are in the macaque. I am reminded of the statements made for a long time by McCulloch and the rest of us that there were no afferent corticocortical impulses to Area 6. (Excuse me if I speak in one terminology and then the other. I caught sight of John Fulton out of the corner of my eye.) After we began to search on the medial surface and in the sulci, we found large numbers of afferent fibers to Area 6. I think, therefore, that if we examine the sulci in the chimpanzee, which we have not done (and a large portion of the cortex is buried in the chimpanzee), we shall probably find plenty of other afferent fibers to FOBM. I am not attempting to elaborate the philosophical implications of this difference of opinion.

I am not sure that there are more areas in the cortex of Galago than there are in the cortex of man. I think Dr. von Bonin meant to say that per unit volume there are more areas. One can find exactly the same areas in the human cortex as in the cortex of Galago. It is only that the percentage of cortex which is generalized in man is far greater than it is in these lower forms.

To my way of thinking, mind is simply a name which we give to the functioning of the cerebral cortex. Perhaps the cortex has to be activated by something deeper in the nervous system, much as a radio tube has to be heated before it begins to conduct, but mind is essentially the functioning of the cerebral cortex.

I have done some experimenting on this system, this heating system, this activating system in the brain stem, in regard to that portion of it which is around the aqueduct. I remember,

when I was attempting, by threading an electrode up into the aqueduct, to destroy the periaqueductal gray matter, that the cat, under pentobarbital anesthesia, yelled bloody murder when the current was turned on, much as Dr. Magoun's cats did when he stimulated in that region. The cats subsided promptly, of course, and after the tissue was destroyed they made no further response of any kind and went into a state which Mr. Cairns called akinetic mutism.

I was very much pleased with the work of Dr. Magoun, as everyone else has been. It has definite bearing upon Dr. Penfield's concept of a centrencephalon. There is good reason, apart from the distribution which Dr. Magoun found in this tissue, to extend Dr. Penfield's centrencephalic zone to include also the reticular substance in the bulb. So far as I know, no one has found a spike-and-dome discharge in, or led off a spike-and-dome discharge from, this region; but there is other evidence. I shall give only one example.

In operating in the posterior fossa, it happened to me, as it sometimes has to other surgeons, that the periosteal elevator slipped and struck the bulb. No obvious damage was done. The patient survived, of course, but immediately, having had a local anesthetic, blacked out, just as have other subjects on such stimulation in the third ventricle or around the aqueduct at the anterior or the posterior end.

I am reminded of experiments on animals that were done by a German surgeon and physiologist, Lenggenhager. With the use of local anesthesia, he exposed the bulb and the upper part of the spinal cord and then pinched them (gently, of course) with his fingers; he found that as soon as he reached the level of the olive the animals blacked out. I think there is good evidence (I could give other sources and sorts of evidence) for extending the centrencephalon down into the bulb, to include the bulbar portion of the reticular formation.

With regard to the beautiful results which Dr. Jasper has obtained with his ingenious method of finding connections between the cortex and the lower nuclear masses, I am very glad indeed to have this confirmation by another method and elaboration of the results obtained by the strychnine method. On the basis of the results obtained by the strychnine method, one would not expect many connections between *OC* and *OA*. One would, however, expect many connections between *OC* and *OB*. So far as I gather, Dr. Jasper has not sought for these connections yet, partly because *OB* is buried in the lunate sulcus. I think that when he begins to search for them he will find plenty of connections between *OC* and *OB*, which is the parakoniocortex, and from which there is a projection from *OB* to *OA*. So that, although there is no direct corticocortical connection between *OC* and *OA*, there is this two-neuron connection, which is very powerful.

I am very happy indeed that Dr. Jasper found connections between the temporal cortex and the thalamus. I always believed there were such connections, but I never was able to demonstrate them by the older methods. Now, that portion of the cortex turns out, as one might expect from its structure, to have connections very similar to those of the rest of the cerebral cortex.

Dr. James L. O'Leary, St. Louis: My comments will relate principally to the papers presented by Dr. Jasper and Dr. Magoun. Dr. Riley has summarized briefly and clearly the salient anatomical features of the reticular substance of the brain stem. This system, if the word "system" is an appropriate cover for its many attributes, has been unusually refractory to study by the experimental anatomical method. Unlike the many systems about which we have extensive knowledge, the axonal links are relatively short and mingle extensively with constellations of cells that in the usual case do not form sharply delimited nuclear aggregates. Thus, it is most difficult to place discrete lesions from which important information can be gleaned by Marchi, Weigert, and Nissl methods. The Golgi method of Ramón y Cajal gives more information, and Lorente de Nó has used it to study the reticular contribution to the vestibulo-ocular reflex arc. Even so, it has limited value for tracing the longer reticular paths, and only the electrophysiological method gives hope of establishing the longitudinal characteristics of the system as it participates in the activity of the entire neuraxis. This is the work which Dr. Jasper and Dr. Magoun and their collaborators are attempting to do.

The extent of the reticular substance rostrally in the neuraxis is indefinite. Most of us are anatomically, rather than functionally, oriented, and confusion arises as soon as we attempt to apply to the thalamus the morphological criteria used to identify reticular components in the lower brain stem. Morphologically speaking, only the reticular nuclei which delimit the lateral thalamic area from the internal capsule satisfy the requirements. To accommodate nuclei of the medial thalamus within the reticular system, electrophysiological data must provide functional

evidence of wealthy connections between brain-stem reticular substance and cerebral cortex via the medial thalamus, and downstream connections between the cortex and the reticular centers. Dr. Jasper and his associates have reported a study of these downstream paths, using the technique of controlled after-discharge to elicit the information. We have used the same method for other purposes and have found it very reliable, for repetitive stimulation of a cortical area which elicits local after-discharge usually leads to activation of related subcortical centers at a significantly lower threshold than that at which spread occurs to adjoining cortical areas. Thus, with carefully controlled stimulation, and with the use of many recording electrodes, it is possible to observe the subcortical terminations of activity propagated from particular cortical areas. Dr. Jasper's results show significant connections of some cortical regions with the centrum medianum, subthalamus, and the reticular substance of the midbrain.

Dr. Magoun has selected the arousal response as an example of a quick generalized change in the pattern of cortical activity which may be occasioned by activation of paths different from those responsible for propagation of specific cutaneous, auditory, and visual impulses to the cortex. Apparently, the brain-stem reticular substance forms an integral link. In this connection, it should be noted that recent anatomical studies by Brodal indicate the existence of a significant spinoreticular path. Thus, other evidence is at hand for the existence of afferent paths passing through the diffusely distributed reticular substance.

In conclusion, a question may be raised as to whether the reticular substance and other adnexa of the midbrain region may not in themselves constitute a sufficient mechanism for accomplishing arousal and other primitive generalized reactions; perhaps these data, too, need to be fitted into Dr. Penfield's concept of a centrencephalon. Nielson and Sedgwick reported the case of an anencephalic infant who lived 85 days and showed arousal and sucking, responses and contentment at coddling, cried at rough handling, and otherwise expressed instincts and emotions. In this case there was no active neural tissue anterior to the midbrain. Evidently, therefore, the reactions were accomplished by no higher integrating mechanism than that available in the brain stem.

Dr. Gerhardt von Bonin, Chicago: The only discussant I have to answer is Dr. Bailey, for he alone discussed my paper. Evidently, I have been too categorical or too short in my abstract. I was not aware that symposium papers had to be discussed.

When I talked about the lack of further differentiation in higher forms, I had in mind largely subdivisions of the cortex of the chimpanzee and of the macaque, which Dr. Bailey, Dr. McCulloch and I studied. We described a number of different areas, particularly in the cortex of the macaque. Our observation on the human cortex convinced us, however, that many of those areas were nice names, given mainly because we could not quite tear ourselves away from Brodmann's terminology, although Lashley and Clark's paper had appeared. We have, I hope, made a step forward in defining a much smaller number of areas than our predecessors.

Dr. Herbert H. Jasper, Montreal, Canada: I should like to apologize to many colleagues who have been working on corticofugal systems in the past for not mentioning their important contributions to this subject, many of which are more significant, perhaps, than the present report, using a new technique.

Dr. Lashley has commented upon the problem that the functions we attribute to the centrencephalic system are subserved by a relatively old portion of the brain stem with few cells. He would ask us to accept the hypothesis that there must be a large number of cells for the type of functions atrtibuted to this system. I have always been impressed with how simple the conscious mind really is, in view of the complexity of neuronal structure of the cortex. Conscious processes seem remarkably simple and of distinctly limited complexity. We are not aware, fortunately, of the detailed events in the complex circuits of the cortex; only greatly simplified meaningful symbols reach the stream of consciousness.

In regard to Dr. Bailey's comments on connections between Area 17 and Area 18 and then Area 19, we have seen these connections from Area 17 to Area 18, but spread to Area 19 did not occurr in our experiments. This unexpected finding has puzzled us very much, since we did get very active subcortical projections under the conditions of our experiments. It would seem that the pathway from Area 17 to Area 19 may involve corticothalamocortical circuits.

I wish to thank Dr. Riley for his comments regarding the anatomical problems presented by this physiological work. Dr. Riley has pointed up the absence of a thalamic reticular system according to traditional anatomy. This is another example of the great difficulty physiologists have in correlating their work with cytoarchitectonic delineation of either the cortex or the brain stem. I have discussed the problem of the thalamic reticular system with several cytoarchitectonic neuroanatomists; some believe that a homologue of the well-recognized mesencephalic and bulbar systems is to be found in the intralaminar nuclei of the thalamus. Others disagree. I believe that part of the system which responds physiologically in this manner had probably better not be included in a reticular system, strictly speaking. We are referring to physiological functions, which may differ from cytoarchitectonic delineations, as is true in many other fields of neuroanatomy and neurophysiology.

Dr. Papez has described recently a connection between the tegmental nucleus of the midbrain and the intralaminar area of the thalamus. This connects at least a part of the mesencephalic system with the thalamic system and may in a sense explain why some similar physiological effects are obtained from the two.

Finally, I should like to close with the comment that our impressions from many years of study of the functional properties of these systems is that the relation is best described in the words of the pioneers in this field, Dusser de Barenne and McCulloch, who spoke of a "functional interdependence" of cortex and thalamus.

ON THE NATURE AND LOCUS OF MIND

STANLEY COBB, M.D.
BOSTON

IT IS NOT my purpose in this paper to aspire to anything new; rather, I wish to expose the sequence of thoughts by which I have somewhat clarified my own thinking about *mind,* in the hope that it will be of use to others. Some people might argue that it is not important to define mind, that it is a concept better taken loosely, left to the philosophers, and not to be belabored by neurologists. In an association of neurologists everyone is interested to find out how the brain works and what it does. Mind is part of what it does. I believe that mind is not an abstraction; it is a thing that we know about by individual experience. But we do not agree as to what the thing is to which we apply the term "mind."

The previous speakers in this symposium have given many anatomical and physiological facts; they have mentioned hypotheses and discussed attention, wakefulness, consciousness, and memory.

RECENT DATA RELATING TO MIND

What are the facts that make it worth while for us to review the concept of mind at this time? During the last quarter-century the following contributions seem to be especially important:

1. *Anatomy.*—The studies in comparative anatomy by such men as Herrick,[1] Brodmann, and von Bonin [2] have brought to us an insight into the correlation of cerebral complexity and the degree of psychological integration as shown by behavior.[3]

2. *Surgery.*—The contribution of the neurosurgeons to the anatomy and physiology of the human cortex has given us a body of facts that is of unparalleled importance. No amount of animal experimentation can take the place of these first-hand observations on conscious surgical patients. The recent book by Penfield and Rasmussen [4] is the outstanding example; Cushing, Förster, and many other surgeons have contributed greatly since the introduction of local anesthesia for crani-

Read at the Seventy-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 18, 1951, as part of a symposium on the "Brain and the Mind."

1. Herrick, C. J.: The Brain of the Tiger Salamander, Amblystoma Tigrinum, Chicago, University of Chicago Press, 1948.

2. von Bonin, G.: Essay on the Cerebral Cortex, Springfield, Ill., Charles C Thomas, Publisher, 1950.

3. Only a few selected references are given, but these furnish further reference to all the data mentioned.

4. Penfield, W., and Rasmussen, T.: The Cerebral Cortex of Man: A Clinical Study of Localization of Function, New York, The Macmillan Company, 1950.

otomy. Penfield's remarkable observations on memory evoked by the stimulating electrode are unique and important. The memories were specific, individual, and usually vivid. Emotion usually seemed to be present. This may be the reason that the neocortex near the rhinencephalon, or the "visceral brain,[4a]" is the part of the cortex from which these memories can be evoked. The background of emotional motivation may be necessary to bring out such evoked recollections. Memory is an essential part of mind, but it is not mind.

3. *Learning.*—Important advances in the understanding of the learning process have been made since the Pavlovian era. Liddell,[5] Gantt, Hebb, Hilgard,[6] Mowrer, and others have contributed to the study of this type of behavior. Especially enlightening has been the work of Lashley,[7] Fulton,[8] and Boycott and Young,[9] who have added anatomical studies to their observations on behavior. Hilgard[6] has pointed out that psychological theories of learning may be developed objectively and self-consistently at the molar level without recourse to hypothetical neurology. He believes, however, that there is a crying need for "a crucial experiment identifying specifically a change in neural tissue (or in bio-electrical fields related to such tissue) as learning takes place." Perhaps Young's[9] experiments on learning and forgetting in the squid are the first answer to this need.

4. *Emotions.*—The understanding of emotions as basic processes, integrated for normal mental performance from the psychological standpoint, is as old as Darwin. More recently Cannon, Bard, Jacobsen, Papez, MacLean, Selye, Wolff,[10] and others have shown the physiological and neurological correlations. The study of the emotions is now a legitimate medical occupation, combining with clinical medicine the anatomy and physiology of the archicortex, the hypothalamus, the autonomic nervous system, and the endocrine glands.[4a]

5. *Neuron Circuits.*—These were first demonstrated anatomically by Ramón y Cajal and later physiologically by Forbes and associates[12] and Lorente de Nó.[13] The concept of reverberating circuits has been of primary importance in bringing physics and mathematics to bear on neurology. The work of Lorente de Nó pro-

4a. Cobb, S.: Emotions and Clinical Medicine, New York, W. A. Norton & Company, Inc., 1950.

5. Liddell, H., in Symposium on Biological Aspects of Mental Health and Disease, New York, Paul B. Hoeber, to be published.

6. Hilgard, E. R.: Theories of Learning, New York, Appleton-Century-Crofts Company, Inc., 1948.

7. Lashley, K. S.: In Search of the Engram in Physiological Mechanisms of Animal Behavior, in Symposium of the Society for Experimental Neurology, New York, Academic Press, 1950.

8. Fulton, J. F.: Functional Localization in Relation to Frontal Lobotomy, New York, Oxford University Press, 1949.

9. Boycott, B. B., and Young, J. Z.: Learning in Octopus Vulgaris, read at the International Physiological Congress, Copenhagen, Aug. 15-18, 1950.

10. Wolff, H. G.: Life Stress and Bodily Disease—a Formulation, A. Res. Nerv. & Ment. Dis., Proc. **29**:1059, 1950.

11. Footnote deleted.

12. Forbes, A.; Cobb, S., and Cattell, H.: Electrical Studies in Mammalian Reflexes: Immediate Changes in Flexion Reflex After Spinal Transection, Am. J. Physiol. **65**:30, 1923.

13. Lorente de Nó, R.: Studies on the Structure of the Cerebral Cortex: Continuation of Study of Ammonic System, J. Psychol. u. Neurol. **46**:113, 1934; Study of Nerve Physiology, Rockefeller Institute of Medical Research, New York, 1947, Vol. 131 (Pt. 1) and 132 (Pt. 2).

vided the data needed by Wiener, McCulloch, and Pitts to develop "cybernetics." Brazier [14] states that "this change in concepts of the nervous system is so great that it is almost impossible to overestimate it. In brief it is a change from the concept of a passive, static nervous system to an active, dynamic one."

6. *Memory.*—Until the theory of cybernetics was promulgated, memory had never been explained by any reasonable physiological theory. Several neurologists had used the concept of reverberating circuits to explain involuntary motor phenomena,[15] emotions,[16] and anxiety, but it remained for Wiener [17] to see that there was an explanation of one type of memory in the great electronic computing machines. The essential fact is that a neuron circuit can be set in action by an incoming single impulse and that the circuit may go on reverberating as long as metabolism supports it, or until other incoming impulses change it. In the electronic computing machines one circuit is set to modify the behavior of the others in response to a certain signal. The circuit stores that reaction; it has been set, and the setting manipulations are the essential past experience. It chooses [18] the proper signal when it comes, having rejected all others. Thus, the appropriate affirmative signal causes the circuit to act in the light of past experience and perform its special function.

7. *Feed-Back.*—Servomechanisms and the theory of feed-back started in the midnineteenth century with Clerk Maxwell and the "governor" on the steam engine. In the last few years radar and self-aiming guns have been the conspicuous examples. As applied to the nervous system, feed-back means that the activity of the reverberating circuits is modified by the return of some of the output of the system as input. Whenever one reaches with his hand for an object, a series of signals flows back (as with the self-pointing gun), through visual, tactile, and proprioceptive receptors, to inform the central mechanism how far the hand is overshooting or undershooting. The amounts of error determine the return input, until the error becomes zero. Such a mechanism to control the search for a goal is called negative feed-back. It accompanies every motor act. Similar mechanisms may be present in the auditory and visual cortical receiving stations. In fact, all intelligent behavior might be explained by such predictive extrapolations. The philosophical implication is of the greatest importance. Teleology becomes an acceptable scientific principle, for one is dealing with a mechanism that allows for purposive behavior. A goal is aspired to and may be reached by means of a feed-back into a reverberating circuit. In other words, choice is acting on the basis of stored past experience (the "memory" of the closed circuit) to cause a volitional act.

8. *Scanning Mechanisms and the Recognition of "Universals."*—As long as the physiological mechanism of visual recognition was postulated as a mosaic pattern

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14. Brazier, M. A. B.: A Neuronal Basis of Ideas, Dialectica **4**:73, 1950.

15. Kubie, L. S.: Theoretical Application to Some Neurological Problems of Properties of Excitation Waves Which Move in Closed Circuits, Brain **53**:166, 1930.

16. Cobb, S.: Borderlands of Psychiatry, Cambridge, Mass., Harvard University Press, 1943.

17. Wiener, N.: Cybernetics, or Control or Communication in the Animal and the Machine, New York, Technology Press, John Wiley & Sons, Inc., 1948.

18. According to H. W. Smith (Organism and Environment, in Adaptation, Ithaca, N. Y., Cornell University Press, 1949), "The recognition of the possibility of choice, is the capstone of the mind."

thrown onto the external geniculate cells and transferred to the occipital cortex, no psychologist could explain how an object seen at a distance could be recognized as the same thing when seen nearby. But a rat has been shown to recognize a square by its shape even when the size and shading are changed, and a man recognizes a letter of print whether it be large or small. The mosaic theory of transmission of a visual pattern could not explain this. Pitts and McCulloch [19] showed that a scanning mechanism, such as is used in television, can scan a letter from top to bottom and compare top with middle and middle with bottom so that the relation of printed (black) area to white area is recorded electrically and can be reproduced. The investigators' researches led them to study the auditory and visual cytoarchitectonics of the mammalian cortex, and they present good evidence that such a scanning mechanism could be present in the cerebrum of man. This might explain how an object is recognized when seen at various distances and from various angles. Moreover, categories appear: Men are recognized as men and birds as birds. Thus, particular impressions call forth universal reactions. So far, the only mechanism known whose existence seems to explain this process is a servomechanism, in a nerve network, with negative feed-back and some sort of group-scanning assembly. Theoretically, nerve circuits, synapses, and nerve impulses, acting according to the all-or-none law, could act as such a mechanism. Herein lies the analogy to the electric computing machine.

THE CONCEPT OF MIND

A series of talks on "The Physical Basis of Mind" have been collected in a little volume edited by Laslett.[20] The book is provocative and full of meat. The philosophers present opposed views. The scientists give interesting observations and theories, led off by a thoughtful, but agnostic, introduction by Sir Charles Sherrington. Adrian tells us "What Happens When One Thinks" in terms of electrophysiology. Slater discusses "consciousness" in a remarkably clear way, emphasizing that it is not a matter of being conscious or unconscious, but of *how* conscious one is. This is a belief I have long entertained[21] and modified from time to time.[22] Consciousness is best conceived of as not synonymous with mind, but as an attribute of mind, one of its component parts. Memory is an equally important component. Without these two one cannot conceive of a mental mechanism. One might name various other components of mind, such as emotion and attention. One thinks of attention as the mechanism that decides which parts of the mass of sensory data shall reach what levels of consciousness. Only a small part, if any, reaches full conscious attention; the others remain more or less conscious.

Slater points out the verbal difficulties inherent in using such terms as "consciousness" and "mind." He believes that "when behaviour reaches a certain degree of complexity it will begin to have a conscious or mental aspect." Gerard,[23] who

19. Pitts, W., and McCulloch, W. S.: How We Know Universals: Perception of Auditory and Visual Forms, Bull. Math. Biophysics **9**:127, 1947.

20. Laslett, P., Editor: Physical Basis of Mind: A Symposium, Oxford, Basil Blackwell & Mott, Ltd., 1950.

21. Cobb, S.: A Preface to Nervous Disease, Baltimore, Williams & Wilkins Company, 1936.

22. Cobb, S.: Foundations of Neuropsychiatry, Baltimore, Williams & Wilkins Company, 1941 and 1948.

23. Gerard, R. W.: Physiology and Psychiatry, Am. J. Psychiat. **106**:161, 1949.

has recently written a remarkable review of the mind-brain problem, covers the physiology, mechanics, and electronics far better than I can. He seems to rely, however, on increased size of brain and number of neurons to explain development of mind, pointing out that the human brain has approximately 10^{10} neurons and saying "a few extra ounces of nerve cells and connections in the cortex have permitted symbolism in language and number, and abstract reasoning to a degree so beyond that of other animals that something almost qualitatively new has been added." I would point out that the honey bee has been shown by Von Frisch [24] to have a sign language that involves symbolism and abstraction. The brain of the bee is minute as compared with that of man. One is persuaded that it is not mere mass of neurons and connections, but something in the type of organization that is more important in constructing the organ of mind.

Russell Brain [20] discussed the important concept of patterns, saying:

> Not only are there twelve thousand million nerve cells out of which the patterns can be made, but nervous patterns exist in time, like a melody, as well as in space. If you look at a tapestry through a magnifying glass you will see the individual threads but not the pattern: if you stand away from it you will see the pattern but not the threads. My guess is that in the nervous system we are looking at the threads, while in the mind we perceive the patterns, and that one day we shall discover how the patterns are made of the threads.

Very well expressed! But not even twelve-thousand million nerve cells could explain a man's thoughts. Too many of these nerve cells are specialized, their functioning preempted by local connections. If the mechanism of memory, habit formation, and conditioning were based on more or less permanent synaptic connections, even the billions of nerve cells available would not be adequate.

Those who believe that each memory has its separate neuron pathway, anatomically conceived, would be thinking of memory as one conceives of the graphology of ideographs. A sign for every thought is too much to believe. But an alphabet of 27 letters arranged and rearranged in different relationships does remarkably well!

A changing dynamic mechanism seems to offer the only tenable hypothesis. It is the integration itself, the relationship of one functioning part to another, which is mind and which causes the phenomenon of consciousness. There can be no center. There is no one seat of consciousness. It is the streaming of impulses in a complex series of circuits that makes mind feasible. Many of these circuits pass from cortex to thalamus and brain stem and back. Probably these are the circuits most important for mental functions; but because it is the working together and the sequence in time that count, no part is higher or lower than the others. Some are concerned largely with alertness and awareness; others, with discrimination and choice.

I would express it this way: The brain is the organ of mind; its great complexity in man makes his thinking possible, but no study of the anatomy and physiology of one brain will ever explain mind. Thinking is a sequence of events, depending on the interplay of messages from one part of the brain to another in response to external stimuli, including messages from other brains. In other words, *mind is the relationship*. If one takes the analogy of thought to a melody, it is

24. Von Frisch: Bees, Their Vision, Chemical Senses and Language, Ithaca, N. Y., Cornell University Press, 1950.

obvious that no amount of histological study, no matter how advanced, could show in a brain more than the pattern left by one note. The sequence of the notes in time makes the melody. Ideas are such sequences.

Such an explanation of mind is not at all new. William James, Bertrand Russell, and Carnap maintained that patterns of relations are all that can be called mind.[2] Von Bonin says:

> To define neurology as the study of the relations of nerve cells is in line with the definition of science by modern logicians as the study of the relations of objects.

Herrick had the same idea when he said, 25 years ago, that two functions were at the basis of all mind, correlation and retentiveness,[25] and that it could be looked upon as "one of the modes of behavior of matter in motion."[26]

Rather than to state as a fact that "mind is the relationship," or offer it as a hypothesis, it would seem more useful to propose a definition. But, first of all, let us get this straight: A definition has nothing to do with fact or truth; it cannot be right or wrong, because it is an optional convention agreed to so that a word can be used to describe a thing. We merely agree that, for this occasion, we will use a certain term (symbol) to refer to a certain object or concept (referant).

I propose that of all the anatomical and physiological properties of the brain touched on in this review, the area most appropriately considered as mind is the integration itself, the relationship of one functioning part of the brain to another. I would so define it, and hope that acceptance and common use of the definition would for a time improve our mutual understanding and advance the science of neurology.

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25. Herrick, C. J.: Introduction to Neurology, Ed. 4, Philadelphia, W. B. Saunders Company, 1924.

26. Herrick, C. J.: Brains of Rats and Men: A Survey of the Origin and Biological Significance of the Cerebral Cortex, Chicago, University of Chicago Press, 1926.

MEMORY MECHANISMS

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"AND WHERE is the place of understanding"? Fifteen years ago, in a discussion of the "Cerebral Cortex and Consciousness,"[1] I began with this quotation from the Book of Job. It states the problem that concerns us in this symposium. Where, as Stanley Cobb has phrased it, is the "locus of the mind"?

My own contribution to this symposium will consist in recent observations on memory mechanisms. But I shall add an interpretation based upon the theorem expressed 15 years ago that the integrating circuits, without which there can be no conscious processes of the mind, are to be found deep within the cerebral hemispheres.

The following observations have gradually accumulated during years of operative treatment of patients who suffer from focal epilepsy. In all cases the patient was fully conscious, under local anesthesia during the exploration of his cerebral cortex.

EVOKED RECOLLECTION

Recollections which are clearly derived from a patient's past memory can sometimes be forced upon him by the stimulating electrode. The psychical experience, thus produced, stops when the electrode is withdrawn and may repeat itself when the electrode is reapplied. Such psychical results have been obtained from stimulation of certain areas of the temporal cortex, but from no other areas of the brain.

A series of brief examples[2] may be given.

From the Department of Neurology and Neurosurgery, McGill University, and the Montreal Neurological Institute.

Delivered as the presidential address at the Seventy-Sixth Annual Meeting of the American Neurological Association, Atlantic City, N. J., June 18, 1951, and forming part of a symposium on the Brain and the Mind.

1. Penfield, W.: The Cerebral Cortex in Man: I. The Cerebral Cortex and Consciousness (Harvey Lecture), Arch. Neurol. & Psychiat. **40**:417-442 (Sept.) 1938; L'écorce cérébrale et la conscience, Ann. psychol., p. 39, 1938.

2. Further details of many of these cases may be found by reference to the patient's initials in the Case Index in the following publications: Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization: A Study of Mechanism, Treatment and Prevention of Epileptic Seizures, Springfield, Ill., Charles C Thomas, Publisher, 1941. Penfield, W., and Rasmussen, T.: The Cerebral Cortex of Man: A Clinical Study of Localization of Function, New York, The Macmillan Company, 1950. Penfield, W., and Jasper, H.: Epilepsy and Cerebral Localization, Ed. 2, Springfield, Ill., Charles C Thomas, Publisher, to be published.

First is the case of S. B.[3] Stimulation at point *19* (Fig. 1) in the first convolution of the right temporal lobe caused him to say: "There was a piano there and someone playing. I could hear the song, you know." When the point was stimulated again without warning, he said: "Someone speaking to another, and he mentioned a name, but I could not understand it . . . It was just like a dream." The point was stimulated a third time, also without warning. He then observed spontaneously, "Yes, 'Oh Marie, Oh Marie!'—Someone is singing it." When the point was stimulated a fourth time, he heard the same song and explained that it was the theme song of a certain radio program.

When point *16* was stimulated, he said, while the electrode was being held in place, "Something brings back a memory. I can see Seven-Up Bottling Company . . . Harrison Bakery." He was then warned that he was being stimulated, but the electrode was not applied. He replied, "Nothing."

When, in another case, that of D. F., a point on the superior surface of the right temporal lobe was stimulated within the fissure of Sylvius, the patient heard a

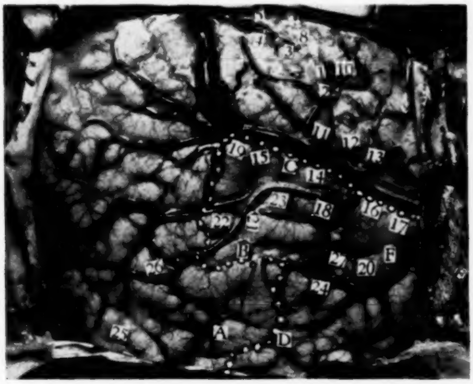

Fig. 1 (Case S. B.).—Operative exposure of right cerebral hemisphere. The large vein passing upward from the fissure of Sylvius drains an arteriovenous aneurysm within the temporal lobe. The numbered tickets indicate points at which stimulation produced positive responses. Tickets 11, 12, and 13 are on the lower end of the Rolandic sensorimotor strip. Letters *A, B, C, D, E,* and *F* indicate electrocorticographic abnormality. The dotted line indicates the amount of the temporal lobe removed in the treatment of the focal epileptic seizures from which the man suffered. See text for temporal lobe responses to stimulation.

specific popular song being played as though by an orchestra. Repeated stimulations reproduced the same music. While the electrode was kept in place, she hummed the tune, chorus, and verse, thus accompanying the music she heard.

The patient, L. G., was caused to experience "something," he said, that had "happened" to him before. Stimulation at another temporal point caused him to see a man and a dog walking along a road near his home in the country.

Another woman heard a voice which she did not quite understand when the first temporal convolution was stimulated initially. When the electrode was reap-

3. This man suffered from seizures introduced by a vertigo and the hallucination that someone was calling his name—"Sylvère, Sylvère." He had an epileptogenic focus in the right temporal lobe.

plied to approximately the same point, she heard a voice distinctly, calling "Jimmie, Jimmie, Jimmie"—Jimmie was the nickname of the young husband to whom she had been married recently.

In these examples it seems to make little difference whether the original experience was fact, dream, or fancy; it was a single recollection that the electrode evoked, not a mixture of memories or a generalization. The electrical current used was often of no greater voltage than the minimum, or threshold, value required to secure responses from the Rolandic sensorimotor cortex.

MEMORY CORTEX

The areas of cortex in which recollections may be evoked are outlined in a general way by stippling in Figure 2. This area, in both hemispheres, might be called

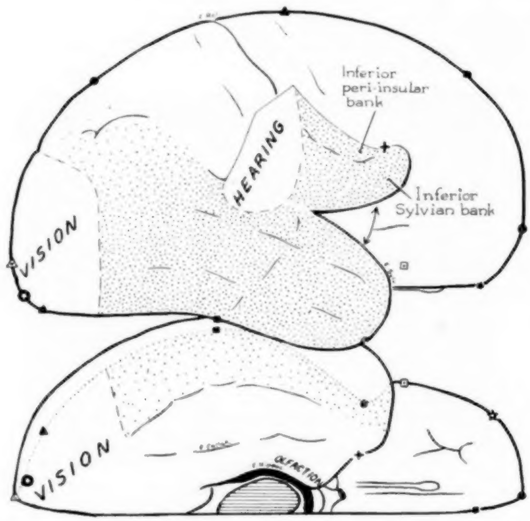

Fig. 2.—Memory cortex, stippled. The superior surface of the temporal lobe is turned upward. The boundary of this cortex, from which stimulation has produced evoked recollections, is not quite certain in the parietal and inferior temporal regions.

the memory cortex, for it is that portion of the cortex in which, under certain conditions, ganglionic activation may cause the patient to be conscious of some specific past experience.

These patients were subject to temporal lobe epilepsy. It is apparent that long-continued conditioning by epileptic discharges in that area of the cortex makes it responsive to stimulation. The recollection produced in a few instances had formed a part of the patient's minor seizures, but oftener these responses bore no resemblance to anything that he or she had experienced during an attack.

COMPARISON WITH OTHER RESPONSIVE AREAS OF CORTEX

Responses from these areas were evoked recollections. They might be visual or auditory, or they might be both. But they differed fundamentally from the visual

or auditory responses produced by stimulation of visual or auditory cortex. Stimulation of the sensory areas of cortex produces results which are peculiar to each area. Somatic-sensation response may be characterized by a tingling feeling, an absence of feeling called numbness, a sense of movement; olfactory sensation, by a disagreeable odor; gustatory, by a strong taste.

From the auditory areas stimulation may produce a buzzing or ringing or knocking sound or a decrease in hearing. But there are no words, no patterned auditory memories.

Stimulation of the visual cortex produces bright, lighted objects, such as stars or squares or streaks, or the opposite, i. e., black forms. It may produce a jumble of colors. The things seen may be stationary, but usually move or twinkle or dance. Thus, the images seen have light, darkness, or color. They have form and movement, but they do not resemble anything which the subject has seen in his environment. He sees no people, no remembered object, no panorama.

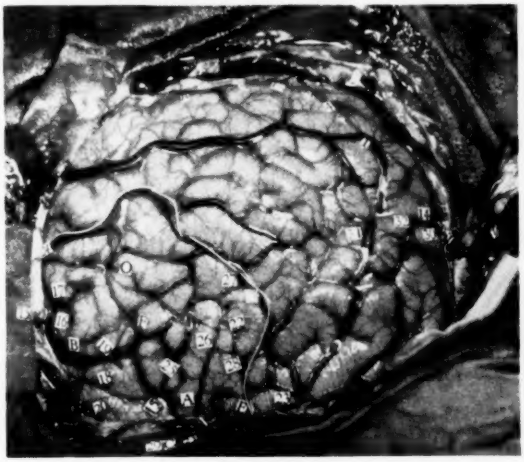

Fig. 3 (Case R. W.).—Posterior half of right cerebral hemisphere. The white thread indicates the line of excision of the occipital lobe in treatment of the focal cerebral seizures. See text for responses to stimulations, marked by numbered tickets. The lettered tickets indicate epileptogenic abnormality detected in the electrocorticogram. Responses in the same case are shown in drawing (Fig. 4).

The responses from stimulation of sensory areas follow what may be called inborn patterns. They are the same regardless of what an individual's past experience may have been. On the other hand, it is obvious that responses from the memory cortex are of an entirely different order. They are made up of the acquired experience of that particular individual.

It is the difference between a simple sound and a conversation or a symphony. It is the difference between the sight of colored squares and the moving spectacle of friends who walk and talk and laugh with you. The one is a simple element of sensation. The other is a recollective hallucination.

The transition from sensory response to recollective hallucination may be abrupt as the electrode is moved over the surface of the cortex. Stimulation points in the case of R. W. are shown in Figures 3 and 4. Mild threshold stimulation at *13* produced a supination movement of the left arm; at *7*, a "pricking sensation" in the left thumb, and at *1*, "a funny feeling in the left lower lip"; with stimulation at *15* he saw "triangles" in front of him, and with stimulation at *16*, "lights and triangles, red, yellow, blue, orange."

Anterior to the line of circles drawn on the cortex, stimulation produced no more crude visual sensations. At *24*, *22*, and *23*, he saw "robbers with guns" and was frightened, as in his habitual attacks. The attacks from which this boy suffered were ushered in by the visual sensory aura of triangles before his eyes, and this was followed by seeing robbers who resembled the figures pictured in the comic books.

Farther forward in the temporal lobe, stimulation produced responses quite unrelated to his seizures. With stimulation at *30* he heard a telephone conversation

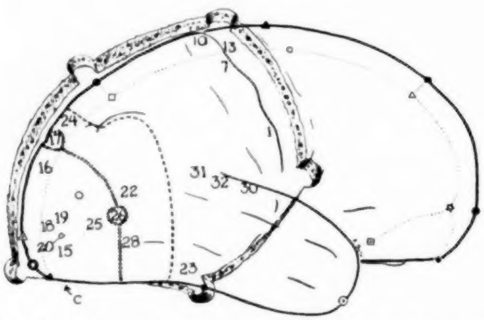

Fig. 4 (Case R. W.).—Stimulation points. The numbers referred to in the text are carried over from Figure 3. The line of small circles separates the visual-sensation responses, posteriorly, from the psychical hallucinations, anteriorly. The broken line indicates the line of lobectomy.

between his mother and aunt. When stimulation was carried out at *31* immediately afterward, he said, "The same as before. My mother telling my aunt to come up and visit us tonight." When he was asked how he knew this was a telephone conversation, he replied that he did not see them but he knew that his aunt was speaking on the phone by the way her voice sounded when she answered. In the original experience he must have stood very close to his mother as she telephoned.

After a lapse of time, point *32*, which was between points *30* and *31*, was stimulated. The recollection mentioned above was apparently no longer available to the electrode. This time he said, "My mother is telling my brother he has got his coat on backwards. I can just hear them." He was asked whether he remembered this happening. "Oh yes," he replied, "just before I came here." He was then asked whether these things were like dreams, and he replied, "No . . . It is just like I go into a daze."

This boy of 12 was an accurate witness. Every effort was made to mislead him by stimulations without warning and warnings without stimulation, but at no time

could he be deceived. When in doubt, he asked thoughtfully to have the stimulation repeated before committing himself to a reply!

ELEMENTS OF EVOKED RECOLLECTION

Under the compelling influence of the stimulating electrode, a familiar experience appears in a patient's consciousness whether he desires to focus his attention upon it or not. A song goes through his mind, probably as he heard it on a certain occasion; he finds himself a part of a specific situation, which progresses and evolves just as in the original situation. It is, to him, the act of a familiar play, and he is himself both an actor and the audience.

The subject feels again the emotion which the situation originally produced in him, and he is aware of the same interpretations, true or false, which he himself gave to the experience in the first place. Thus, evoked recollection is not the exact photographic or phonographic reproduction of past scenes and events. It is reproduction of what the patient saw and heard and felt and understood.

In many cases, it has been evident that the evoked memory is more detailed than anything the patient could possibly summon for his own consideration. It is not fused with other, similar experiences. In this respect evoked recollection differs from normal recollection of the past, where single experiences may be indistinguishable from other, similar experiences.

This is illustrated by the case of Mrs. G. F., a very intelligent housewife. After a point in her temporal cortex had been stimulated, she observed with some surprise, "I just heard one of my children speaking." Then she added, "It was Frank, and I could hear the neighborhood noises." When asked, she explained that by neighborhood noises she meant such things as automobiles passing in the street. When the point was restimulated, she heard the neighborhood noises but not Frank.[4]

Ten days later I discussed her operative experience with her. Referring to the result of the stimulation just mentioned, she said that it was not like a memory. "It seemed more real than that. But, of course," she added, "I have heard Frankie like that many, many times, thousands of times." Mrs. G. F. probably could not, if she wished to do so, single out one of the many times she had heard her son playing outside the house. She would have to generalize in regard to many such experiences. She listened for him always, and naturally she feared that he might get into the street and be run over. Consequently, she was in the habit of focusing her attention on the neighborhood noises, as well as Frankie. She recognized the situation evoked by stimulation as authentic, but "more real" than a memory.

J. T. was startled when, as the result of temporal stimulation, he heard, as he lay in the operating room, the voices of his "cousins Bessie and Ann Wheliow," so that he cried out, "Yes, Doctor, yes, Doctor. Now I hear people laughing—my friends, in South Africa." It was obvious that this experience seemed to him different from an ordinary recollection. It forced itself upon his attention suddenly and unexpectedly.

When he reconsidered the matter a fortnight later, he said it had seemed to him that he was with his cousins and that they were all laughing together at something, although he could not say what the subject of their merriment might be. The recollection, as far as it went, was vivid and detailed.

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4. Between the two stimulations she had been questioned about the neighborhood noises. One is tempted to believe that this increased the availability of such a recollection.

He did not feel inclined to laugh at the joke, whatever it may have been. He was, somehow, doubly conscious of two simultaneous situations. His exclamation showed his immediate appreciation of the incongruity of the two experiences—the one in the present, and the other forced into his consciousness from the past. He made a memory record of this strange experience, perhaps by using the contralateral temporal cortex, for his postoperative memory of the event was clear. Here, again, the evoked experience was more vivid than an ordinary memory. It was as clear as it would have been 30 seconds after the original experience.

Thus, it would appear that the memory record continues intact even after the subject's ability to recall it disappears. Recollection which is evoked from the temporal cortex retains the detailed character of the original experience. When it is thus forced into a patient's consciousness, it seems to him to be a present experience, possibly because it forces itself so irresistibly upon his attention. Only when it is over may he recognize it as a vivid memory of the past.

In contrast to this, if he had tried to recall such a specific memory, he might have been unable to do so. He might only have been able to generalize in regard to a series of similar experiences. During the evoked recollection he hears an orchestra playing an air, or he hears a voice singing it. But if he makes a voluntary effort, it may be that he can recall only the air and the words of the song, but not the detail of each hearing. When he has learned the song, he generalizes from his past experiences.

It should be pointed out that these observations throw no light on memory of words. Stimulation never causes a patient to speak, nor does it call to his mind separate words.

In the dominant hemisphere there are discrete areas which may be called speech areas—in the frontal, the temporal and the parietal lobes. Stimulation in one of these areas interferes with the speech mechanism, so that the patient finds himself to be aphasic if he tries to speak. If he does not try, he is not aware of the stimulation. My associate, Dr. Lamar Roberts,[5] will discuss this subject later in this meeting.

RECORDING AND RECALL

These results of stimulation prove the existence of memory patterns; but how are they formed there, and how are they used? The answers to those questions are of great psychological importance, and I propose to venture from the firm ground of observation onto the dizzy scaffolding of hypothesis.

In order to propose a reasonable explanation of the recording of present events and the subsequent recollection of them, it is necessary to assume the existence of an integrating system outside the cerebral cortex and in equal functional contact with the cortex of both hemispheres.

The Centrencephalic System.—Much recent work suggests that there is a neurone system centrally placed within the brain and equally connected with the two hemispheres. The evidence indicates that this system is situated in the stem of the encephalon, the brain stem; and one may consider the brain stem to include the thalamus, according to the definition of Herrick. Magoun and Jasper have

5. Roberts, L.: Localization of Speech in the Cerebral Cortex, Tr. Am. Neurol. A., 1951.

brought forward evidence in this symposium to indicate that this centrally placed system is provided with widespread connections to and from the cortex of both hemispheres.

In any case, let us assume that there is an interhemispheral functional system. We might describe the system as biencephalic, but perhaps centrencephalic is more descriptive. I have proposed this term as the result of repeated discussions, especially with Stanley Cobb and Herbert Jasper.

Let us define the centrencephalic system as that neurone system in the higher brain stem which has been in the past, or may be subsequently, shown to have equal functional relations with the two cerebral hemispheres.

I have pointed out elsewhere [1] that evidence derived from the study of the effect of brain lesions and the study of epileptic mechanisms indicated that "the indispensable substratum of consciousness lies outside the cerebral cortex, probably in the diencephalon."

Other neurologists, particularly the neurosurgeons (Fulton and Bailey,[6] Cairns and associates,[7] Dandy,[8] Jefferson and Johnson [9]), have been driven by clinical experience, sometimes sad experience, to conclude that paralyzing lesions near the third ventricle and higher brain stem produce unconsciousness, while lesions, however large, which are restricted to the cerebral cortex do not abolish consciousness, although they may modify its content. We may accept for the purposes of further discussion that there is a centrencephalic neurone system functionally related to both hemispheres and according to the work of Jasper, Ajmone-Marsan and Stoll,[10] functionally related to the temporal cortices, as well as to other areas.

We may assume, since the integrity of the higher brain stem is essential to the very existence of consciousness, while other areas are not, that the centrencephalic system, which is situated there, is in some way related to those intellectual processes which would be possible only in the presence of final integration of the functions of the nervous system.

Now, to return to a consideration of memory mechanisms, the records of an individual's thinking lie dormant in the patterns of his temporal cortex until he activates them in some normal process of recall or until they come into spontaneous, and perhaps distorted, existence in his dreams.

Whenever a normal person is paying conscious attention to something, he is simultaneously recording it in the temporal cortex of each hemisphere.[11] Every

6. Fulton, J. F., and Bailey, P.: Tumors in the Region of the Third Ventricle: Their Diagnosis and Relation to Pathological Sleep, J. Nerv. & Ment. Dis. **69**:1-25, 145-164, 261-277, 1929.

7. Cairns, H.; Oldfield, R. C.; Pennybacker, J. B., and Whitteridge, D.: Akinetic Mutism with an Epidermoid Cyst of the Third Ventricle (with Report on Associated Disturbance of Brain Potentials), Brain **64**:273-290, 1941.

8. Dandy, W. E.: Location of Conscious Center in Brain—Corpus Striatum, Bull. Johns Hopkins Hosp. **79**:34-58, 1946.

9. Jefferson, G., and Johnson, R.: The Cause of Loss of Consciousness in Posterior Fossa Compressions, Folia psychiat. neurol. et neurochir. neerl. **53**:306-319, 1950.

10. Stoll, J.; Ajmone-Marsan, C., and Jasper, H.: Corticofugal Projections to the Brain Stem, Tr. Am. Neurol. A., 1951; A. M. A. Arch. Neurol. & Psychiat. **67**:155 (Feb.) 1952.

11. There are various reasons for considering this a bilateral identical process, the most important being the fact that unilateral excision of the temporal cortex from which a recollection has just been evoked by stimulation does not abolish the patient's memory of the event recalled.

conscious aspect of the experience seems to be included in these cortical records. I have called the record a ganglionic pattern, for lack of a better phrase. The arrangement of ganglion cells and their synaptic connections must form a relatively stable endowment, changing little with the passage of time. But the pathway of impulse from one cell to another through synaptic barriers—this may constitute the new-formed pattern, provided the facilitation produced by the passage of impulses has some permanence.[12]

When the electrode is applied to the memory cortex, it may produce a picture, but the picture is not usually static. It changes, as it did when it was originally seen and when the subject perhaps altered the direction of his gaze. It follows the originally observed events of succeeding seconds or minutes. The song produced by cortical stimulation progresses slowly, from one phase to another and from verse to chorus.

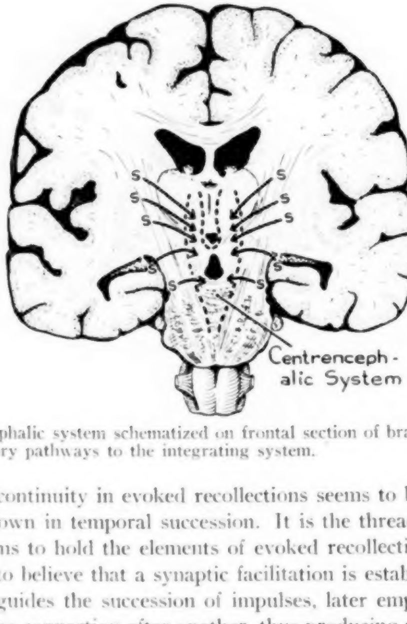

Fig. 5.—Centrencephalic system schematized on frontal section of brain. The lines marked *S* indicate various sensory pathways to the integrating system.

The thread of continuity in evoked recollections seems to be time. The original pattern was laid down in temporal succession. It is the thread of temporal succession that later seems to hold the elements of evoked recollection together.

It is tempting to believe that a synaptic facilitation is established by the original experience which guides the succession of impulses, later employed to activate the pattern, through one connection after another, thus producing recollection. Synaptic facilitation is an excellent phrase, which may serve the purposes of hypothesis. But it is obvious that years of study will be needed to define its nature.

Hypothetical Mechanisms.—The recollection that is evoked by stimulation of one temporal cortex contains visual and auditory elements fused together into a single concept. One is never normally aware of the hemianopic picture that the

12. Eccles and McIntyre (Plasticity of Mammalian Monosynaptic Reflexes, Nature **167**: 466-468, 1951) have shown that there is a plasticity even in monosynaptic reflexes that gives permanency to the effect of the passage of impulses. They suggest that this forms the basis of learning and memory.

visual area in one hemisphere might provide. The visual areas, like the other sensory areas of each hemisphere, are way-stations between the periphery and the central integrating system. In Figure 5, the centrencephalic system is schematized, and the converging pathways of sensation are indicated by the arrows marked *S*. These pathways have reached the cortex and now converge as they pass on. Only the pathway of pain makes no essential detour to the cortex. Its way-station is in the thalamus.

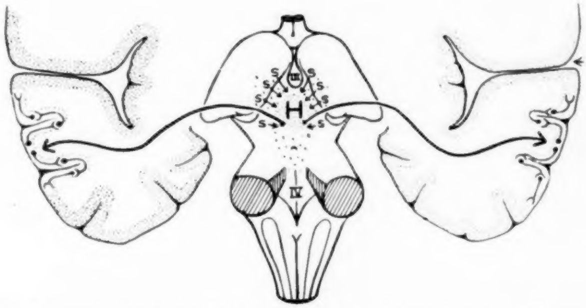

Fig. 6.—Schematic drawing of higher brain stem and frontal section of temporal lobes showing establishment of memory patterns. *H* indicates an unlocalized area of the centrencephalic system which is concerned with recording.

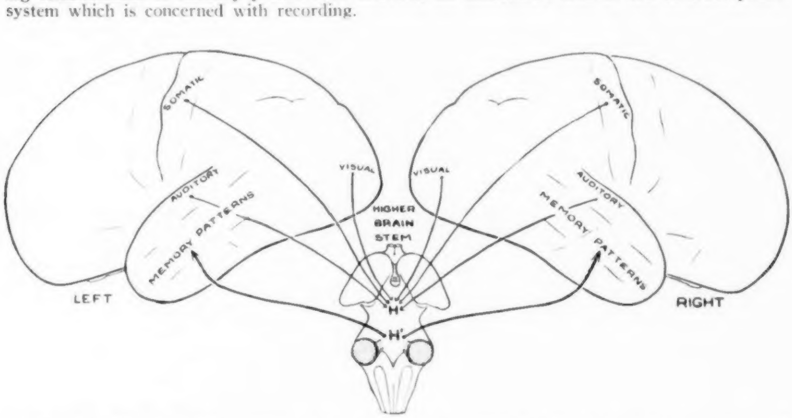

Fig. 7.—Diagrammatic representation of sensory projection to higher brain stem and memory projection to cortex of temporal lobes.

I would assume, then, that only in this centrencephalic system can summary and fusion of all types of sensation be achieved. Only from here, at all events, could the recording nerve impulses be projected to the temporal cortex of each side.

This projection probably reaches the temporal cortex of either side by some such course as that indicated by the heavy lines in Figure 6. In this figure the letter *H* is meant to indicate only that portion of the centrencephalic system (wherever it may be) which is most intimately related to the memory cortex of the temporal lobes.

The recording projection seems to carry with it only those sensory elements to which the individual was paying attention, not all the sensory impulses which are forever bombarding the central nervous system. Constant selection is made, a selection which is determined by the focusing of the individual's attention. This conception of the process of recording is illustrated somewhat differently in the diagram in Figure 7.

The recording projection therefore carries with it a very small proportion of the total sensory information available at the "highest level," but it also carries with it other important psychical elements. Among these elements are included understanding of the meaning of the experience, and the emotion it may have aroused. These elements could be added to the stream of projection only in this area of final integration, which is in direct functional contact with speech areas of the cortex and with frontal and parietal lobes, as well as sensory areas.

Let us turn now to the electrical production of recollection. Take, for example, the case of D. F., referred to above. After the removal of the anterior end of the right temporal lobe, stimulation of the cut surface of the gray matter at point *23*

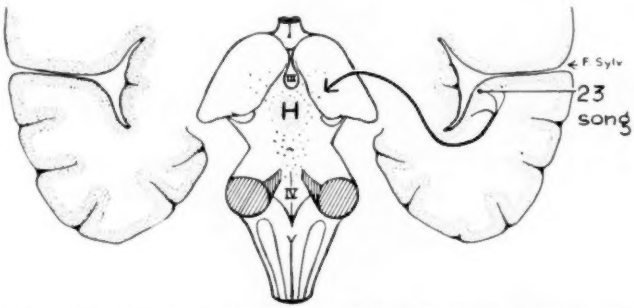

Fig. 8 (Case D. F.).—Repeated stimulations at point 23 caused the patient to hear a specific song played by an orchestra on each occasion.

(Fig. 8) caused her to hear the popular song, "Marching Along Together." Over and over again she was forced to hear it, as though it were played by an orchestra. Whenever the gentle electrical current was reapplied there, she heard it again.

Thus, an electrical current consisting in 60 pulses per second caused her to hear this music. It progressed at the ordinary tempo, so that when she was asked to explain what she heard, she hummed it through in time with the music. It seems reasonable to suggest that a memory pattern was being activated and that she was conscious of the music because of neurone impulses that passed from the "pattern" in the temporal cortex to the centrencephalic system. The suggestion which I make is that these impulses pass in the reverse direction to those which created that pattern when she first heard the music.

I would suggest that during any evoked recollection the flow of electricity may activate a ganglionic synaptic sequence, as suggested by diagram in Figure 9. This is probably somehow projected from the temporal cortex into the central integrating system, for if the original experience could reach conscious consideration only by passing through the central integrating system, it is likely that this reproduction

of the experience would have to be projected back into some part of the same system in order to reach conscious consideration.

If the foregoing hypotheses are correct, then how does the individual himself summon the memory on what may be called a voluntary basis? It is obvious that one preserves the capacity to recall an individual experience more or less perfectly for a short period of time after the event.

It would seem reasonable to suggest, then, as in Figure 10, that this recall is carried out by nerve impulses which follow a course from the centrencephalic system to both temporal cortices in a pathway similar to that originally followed by the impulses that laid down the memory pattern thus in duplicate.

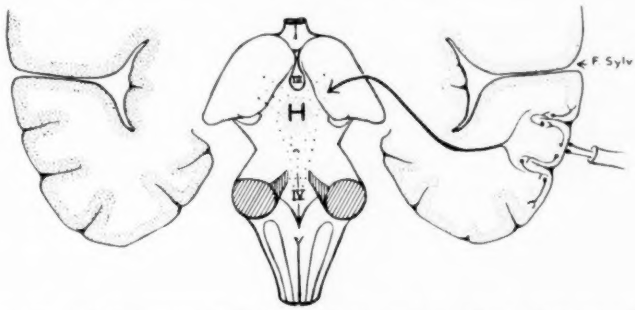

Fig. 9.—Theoretical representation of a ganglionic memory pattern which was activated by a stimulating electrode, applied to one temporal cortex.

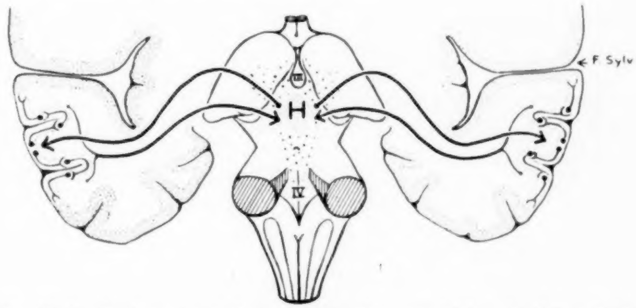

Fig. 10.—Higher brain stem and frontal section of temporal lobes showing voluntary activation of memory patterns.

But I would urge you to understand that this does not mean a highest level of integration divorced from the cortex. On the contrary, it should be clear that the cortex contains areas such as the memory areas, which are specialized so as to elaborate the function of the subcortical integrative system. Neither zone can function independently.

We may now compare voluntary recollection with evoked recollection (Figs. 9 and 10). There seem to be certain important differences in the memories recalled by the two methods, as I have pointed out, and these differences become greater with the passage of time.

Let us consider a well-remembered song. It was evoked by a steady series of electrical impulses delivered to a small area of cortex. It might seem likely that a steady or interrupted stream of corticipetal neurone impulses delivered to the same area from a subcortical source would activate the same ganglionic pattern and cause a corticofugal stream of impulses to project the memory back to the centrencephalic system, thus reaching consciousness.

The utilization of any other mechanism of memory recall would mean that this highly specialized function was provided with two separate mechanisms, and this seems unlikely, to say the least.

We may conclude, then, that a man who has a good repertoire of remembered music, after he has selected one song, may hear it played through in his own "mind" by causing impulses to pass down ganglionated nerve chains to the temporal cortex. The song will continue until he turns his attention elsewhere and shuts off those nerve impulses.

This would seem to be absurdly simple, and yet the new evidence is inescapable—that electrical impulses at a point on the surface of the cortex are sufficient to activate a complicated memory sequence—and this makes it seem plausible that all the memories we can recall have each a separate neurone pathway. Furthermore, those neurone pathways may be activated voluntarily.

It is obvious that what may be called voluntary memory is a generalization which may be progressively modified with the passage of time. The difference between the evoked recollection and ordinary recollection is important, but time does not permit the presentation of further examples for comparison.

INTERPRETATION OF PRESENT EXPERIENCE

It should be pointed out that the temporal cortex is obviously utilized in the interpretation of current experience. Every clinician is aware that minor epileptic seizures which involve the temporal region may produce misinterpretation, an illusion of interpretation. For example, the patient may have the sudden feeling that this has all happened before, the déjà vu phenomenon.

Illusions of this and other types may be produced by stimulation of the temporal cortex, as well as by local epileptic discharge. The disturbance produced is one of judgment in regard to present experience—a judgment that the experience is familiar, or strange, or absurd; that distances and sizes are altered, and even that the present situation is terrifying.

These are illusions of perception, and a consideration of them leads one to believe that a new experience is somehow immediately classified together with records of former similar experience so that judgment of differences and similarities is possible.

For example, after a period of time it may be difficult for a man to conjure up an accurate, detailed memory of an old friend, as he appeared years ago, and yet when the friend is met, however unexpectedly, it is possible to perceive at once the change that time has wrought. One knows it all too well—new lines in his face, change in hair, stoop of shoulder.

CONCLUSIONS

The discovery of the fact that recollection may be evoked by stimulation of the human cortex is no less important than the original discovery that stimulation of

the animal cortex would produce movement. It has, of course, long been known that minor epileptic discharge might call to mind a memory or produce an illusion of recollection, just as Jacksonian motor seizures were familiar long before Fritsch and Hitzig stimulated the dog's cortex. But the fact that threshold stimulation may reproduce the substance of a man's earlier conscious thinking without after-discharge or epileptic spread opens a door into a new chamber of understanding.

From the consideration of new facts such as this it is natural to turn to theories of mechanisms. I have spoken vaguely of a hypothetical integrating system and have given it the name centrencephalic for purposes of convenience. But recent studies, such as those of Magoun [13] and of Stoll, Ajmone-Marsan, and Jasper,[10] which we have heard this morning, give us direct evidence concerning the functional activity of this system.

If anywhere, it is in the centrencephalic system that Hughlings Jackson's "highest level" of functional integration is to be found. But the circuits of this system run out to the various functional areas of the cortex and back again. The memory cortex forms one of these areas. In a very real sense, there is no "higher" and no "lower" in this system. The "place of understanding" is not walled up in a cell or in a center of gray matter. It is to be sought in the perfect functioning of all these converging circuits.

The demonstration of the existence of cortical "patterns" that preserve the detail of current experience, as though in a library of many volumes, is one of the first steps toward a physiology of the mind. The nature of the pattern, the mechanism of its formation, the mechanism of its subsequent utilization, and the integrative processes that form the substratum of consciousness—these will one day be translated into physiological formulas.

But when that day dawns, I surmise that men will still stand in doubt before the ultimate riddle—What is the bridge between nerve impulse and thought? And what about a man's soul?

DISCUSSION ON PAPERS BY DRS. COBB AND PENFIELD

Dr. Lawrence S. Kubie, New York: I am profoundly grateful for this opportunity to discuss Dr. Penfield's paper, not only because the honor is undeserved, but also because of the enormous stimulation which the paper itself has given to my imagination. Indeed, it has kept me in a state of ferment for the last two weeks, watching pieces of a jigsaw puzzle fit into place and a picture emerge to throw light on some of the work which I have been doing in recent years. For me personally, this has been as exciting a moment as I have spent in a scientific meeting in recent years. I can sense the shades of Harvey Cushing and Sigmund Freud shaking hands over this long-deferred meeting between psychoanalysis and modern neurology and neurosurgery, through the experimental work which Dr. Penfield has reported. I venture to guess that Dr. Penfield may feel no little surprise at the role which he is playing so unexpectedly.

In the few minutes that are available for this discussion, I am not sure that it will be possible to make clear just why this paper has excited me so. But when we realize that almost everything we know about the neurotic process—its etiology, its therapy, and its prevention—is related to the fate of hidden memories, perhaps the importance of this work will become clear.

I shall confine my discussion largely to that section of Dr. Penfield's paper which deals with his observations, rather than the equally fascinating later section, on the centrencephalic system. I limit myself in this way only that I may remain within the prescribed time limits.

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13. Magoun, H. W.: An Ascending Reticular Activating System in the Brain Stem, Tr. Am. Neurol. A., 1951; A. M. A. Arch. Neurol. & Psychiat. **67**:145 (Feb.) 1952.

Dr. Penfield's observations dissect the processes of memory into three major categories: (1) recording, (2) recalling, and (3) reliving. In other words, they deal not only with the conceptualizations which we build out of fragments of recollections regrouped and re-represented, but also with the direct sensory reexperiencing of past external experiences (exteroceptive) and of our own somatic participation in these past experiences (enteroceptive).

A. The recorded fragments can be recovered in a form that Dr. Penfield calls "recollective hallucinations." These are produced by electrical stimulation of those areas of the cortex which are specific for each sensory modality. This would correspond to Orton's first platform of sensory reception in his analysis of language function (Orton, S. T.: Reading, Writing and Speech Problems in Children, W. W. Norton & Company, Inc., 1937).

B. In contrast to this, stimulation of certain areas of the temporal cortex evokes organized recollections of specific events. These electrically evoked recoveries of the past can occur with various degrees of organization and different qualities and attributes.

1. They may be evoked as though they were immediate and present experiences. The song goes through the mind, "as he heard it on a certain occasion. . . . [The subject finds himself in a situation which] progresses and evolves just as in the original situation. . . . [It is] the act of a familiar play, and he is himself both an actor and the audience, [the subject feeling] doubly conscious of two simultaneous situations. . . . He is in a dual role, in that he is at the same time in the experience and outside of it and observing it. . . . Frequently the evoked experience was more vivid than an ordinary memory." All this is the very stuff of dreams.

2. The next type of recovery of the past is less vivid than the first, yet still vivid in its own way. This is when images are evoked as past sensory experiences, but with limited participation by the bodily components of the subject's responses. This recovery is an exteroceptive sensory image of the past, more vivid than a purely verbal memory, but less vivid or imminent than a full reactivation or reliving or reevocation of the past. It is close to the type of sensory memory which can be evoked in hypnagogic reveries (Kubie, L. S.: *Bull. Menninger Clin.* **7**:172-182 [Sept.-Nov.] 1943. Kubie, L. S., and Margolin, S.: *Am. Neurol. A.* **68**:136-139, 1942).

3. The third type of memory is mediated by verbal symbols of past events, rather than through vivid sensory images. This is how we ordinarily call up our memories for ourselves, without the aid either of electrical stimulation or of hypnagogic dissociation. As Dr. Penfield indicates, it is of fundamental importance that "electrical stimulation of a so-called speech area never causes a patient to speak, nor does it call to his mind separate words, but rather interferes with the speech mechanisms and produces aphasic disturbances." In this connection, however, one must call to mind Brickner's observation of the patient in whom perseverating speech patterns could be produced by stimulation of a certain cortical area on the mesial surface of the brain (Brickner, R. M.: *J. Neurophysiol.* **3**:128-130 [March] 1940).

From all of this work we learn that at least in certain epileptic subjects the electrical stimulation of the temporal cortex can produce the equivalent of hypnotically induced regressions into the past, with a reliving of the past as though it were the present. It is important that this can occur both on the operating table and in the experimental psychological laboratory. Here is a proof that the past can be as vivid as the present; or that, as Freud put it, in the unconscious there is no such thing as time and space. It proves also the literalness with which past moments are permanently stored as discrete units (Spiegel, N.; Shor, J., and Fishman, S.: An Hypnotic Ablation Technique for the Study of Personality Development, *Psychosom. Med.* **7**:273, 1945).

In such evoked memories the individual is not merely an observer of vivid sensory imagery. The past "seems to him to be a present experience because it forces itself so irresistibly upon his attention," and he gives full somatic participation to the experience. He is there in the flesh, as well as in the mind. This is archipallial, as well as neopallial, memory. This is Proust on the operating table, an electrical *recherche aux temps perdu*. Yet is it *perdu*? It will be important for Dr. Penfield and his group to ascertain how often the recovered experiences were forgotten (repressed) memories. Furthermore, the whole observation may be related to the eruption of buried memories, which sometimes occurs after the convulsions which are induced by electric shock therapy.

Evidently, in this work Dr. Penfield has described the most important kind of evocation of the past which is known to us; and there is no limit to the possible value of his observations for the future development of psychotherapeutic techniques through their interrelation with neurophysiology. Because of this great potential importance in another field, I want to stress the differences between the characteristics of these relived experiences, which are at one end of the spectrum, and which are evoked by the direct electrical stimulation of the temporal cortex, as contrasted with the characteristics of memories which are mediated by the verbal symbols of generalizations from many past experiences.

The first is obligatory. It is directly sensory and nonverbal. The subject is both the observer and the observed. He participates fully with all of his somatic and emotional response, thus reliving the internal quality of the experience (the I component), as well as the external event (the non-I component), i. e., all that "the patient saw and heard and felt and understood." In short, his archipallial, as well as his neopallial, reservoirs are tapped. The recall is essentially total, involving far more than he is consciously able to recapture, approximating that totality of recall which can sometimes be achieved with patients under hypnosis. Intervals in time and space have no importance, the past being as imminent and as vivid as the present. Finally, what is evoked is a specific reliving of a specific experience, and not a diffuse "memory" of nonspecific generalizations from many past experiences. In short, the electrical stimulation of these areas of temporal cortex can evoke in a few moments precisely that type of reexperiencing of the past which the analyst has to struggle for days and weeks and months and years to achieve.

This observation may shed light on one of the critical limiting factors in psychoanalytic therapy; or, to put it in more general terms, it may explain a limiting factor in the psychotherapeutic leverage of any form of psychotherapy which depends upon the use of words to recapture "memories" in the pursuit of "insight." In general, it is true that words can evoke only verbal symbols of past events. Therefore, whenever the acquisition of insight depends on the use of words to recapture related verbal memories, the psychotherapeutic process becomes involved in an unceasing struggle to circumvent this obstacle, so as to bring the patient to a more direct and intimate reliving of his past experience. The analyst often fails to get around this difficulty.

If I may permit myself a hopeful glance into the future, I should like to predict some future studies founded on this work. It is always a presumption to suggest to a colleague that he undertake specific tasks in his own field. In this instance, however, since the suggestions come from a very different sister-discipline, and since their purpose is both to round out a magnificent piece of work and to bring the two disciplines closer together, it may be permissible.

1. Precise studies of verbatim recordings of current dream material and of the free associations of these patients during a period of preoperative psychoanalytic survey might be illuminating in several ways. They might bring to light the latent emotional storm centers of these patients for later comparison with the material produced on the operating table; and they might establish in each case the normal base-line patterns, rhythms, and speed of the spontaneous processes of free associations, also for later comparisons.

2. These observations would be enriched by the use of a suitable battery of psychological tests.

3. In certain instances, it might be desirable to make supplementary preoperative studies of what could be released under the influence of various narcotics and other dissociative agents and maneuvers (such as hypnosis), together with a recording of the patterns of free associations during such maneuvers.

4. A careful comparison of all such preoperative data with everything which would be produced on the operating table during electrical stimulation of the cortex (both focal and diffuse stimulation) might illuminate many problems concerning the central representation of unconscious conflicts and of unconscious psychic processes in general.

5. Finally, it would be interesting to compare preoperative and postoperative neurotic symptom, dream material, free associations, and psychological tests in patients whose temporal lobes have been stimulated on the operating table, but from whom there have been no focal extirpations or ablations, to see whether the reliving of the past through electrical stimulation of the temporal cortex exercises any influence on preexisting neurotic symptoms and mechanisms, and on preexisting associative patterns and emotional storm centers.

I cannot omit asking a few questions which have occurred to me as I have studied this work.

1. In view of the importance of the archipallial components of memory and of the close tie-up of the temporal lobe system with the smell brain, and in view of the role of smell and taste in all temporal-lobe procedures, one wonders about the role of olfactory and gustatory components in memories induced by electrical stimulation. One would expect these to be central in all archipallial memory traces in any form of "gut memory."

2. It is also of considerable interest to know whether auditory and visual components are quantitatively equal in the sensory memories evoked by direct cortical stimulation. We know that in dreams and hypnagogic reveries among the distance receptors visual imagery plays a leading role. From Dr. Penfield's descriptions, it is not possible to make a quantitative comparison, but one gets an impression that in the electrical stimulation of the temporal lobe auditory imagery plays the major role. A precise quantitative study of this material to determine the representation of the various sensory modalities (both distance and proprioceptive receptors) would not fail to be important. This would require the recording of fairly long, random samples of the material, and its subsequent quantitative analysis.

3. There is in this work a suggestion that memory material is stored in the brain in more than one way: more specifically, that it must be stored in patterns of verbal representation, as nonspecific generalizations from discrete experiences, and with a predominantly intellectual, neopallial, and relatively nonemotional content, while, at the same time, there is also the storing of the more precise, specific, "gut" memories, with vivid sensory components of various kinds. The verbal, or neopallial, memory seems, then, to serve as a screen memory, which covers the sensory, or "gut," memories of the same experiences. Much of the whole problem of insight and of psychotherapy depends upon our ability to penetrate that screen; and the study of this material from this point of view seems to this discusser to be of paramount importance.

Dr. Penfield's work opens up many other important fields, which, in my limited time, I can only mention.

In quick parenthetical phrases and strokes as brief as a Marin painting, Dr. Penfield points to the evidence that the indispensable substratum of consciousness (and, indeed, of all conscious psychic activity) lies not in the cerebral cortex but in the diencephalon, especially in areas around the third ventricle and the higher brain stem. He indicates also that there is evidence that conscious attention requires "simultaneous recording and identical ganglionic patterns in the temporal cortex of both hemispheres." This raises several questions, e. g., what happens in unconscious recording, and what happens in the reverse phenomenon, i. e., when emotion-laden experiences are pushed out of conscious memory to an area of neurophysiological representation where they are no longer accessible to direct conscious self-examination, and yet where they continue to influence behavior? The ultimate answer to these questions will throw light on the neurophysiological mechanisms by which emotions influence the processes of recording, of recalling, and of reliving. When this is added to our understanding, then the whole subtle and important story of the neurophysiology of the unconscious and of repression will begin to unroll before us. Toward this goal, the work of Dr. Penfield is making a critical contribution.

Dr. H. Houston Merritt, New York: We are all exceedingly fortunate in being present at this symposium on the relation of the brain and the mind. It is a distinct step forward in the field of neurology. Neurology has long been criticized because it has not been able to show any relation between the brain and the mind and because it has not been able to give physicians, particularly psychiatrists, any direct insight into the neural mechanism of the mental symptoms which are present in their patients.

The papers presented this morning have not answered the problem *in toto*, but there have been great steps forward. The anatomicophysiological studies, the presentation of Dr. Cobb, and the extremely interesting studies of Dr. Penfield, bring us nearer to the goal.

Dr. Penfield emphasized that the cortical sensory areas are not the centers of consciousness and they are not the centers that really recognize the stimuli that are introduced. These so-called projection areas must be supported by the association areas. The anatomical studies and Dr. Penfield's studies showed that practically all of the association areas are involved in memory mechanisms and in the referring of relays to the lower centers. Strangely enough, the frontal lobe, which is considered one of the highest association areas, did not evoke any memory

responses when stimulated by Dr. Penfield. Also, there are no significant connections between the frontal lobe and the lower reticular formation. This observation may bear some relation to the fact that the frontal lobotomies do not give any great impairment of memory.

The studies that are now being conducted on the relation of the temporal lobe to psychomotor epilepsy may lead to a better understanding of the relation of the temporal lobe to memory and to recall. The animal studies that were presented lend a great deal of support to Dr. Penfield's suggestion that the centrencephalic centers serve as relay centers by which impressions are received and discharges are sent back to both temporal lobes.

It seemed somewhat odd to me that none of the patients cited by Dr. Penfield reported any olfactory associations with the recalled memory patterns. It is strange, because olfaction is acutely tied up with memory. All of us know that a familiar odor brings back very vividly the experiences of the past. I should like to ask Dr. Penfield whether he has any information on this point. Was the absence of olfactory associations in the memories elicited due to the fact that stimulation was limited to the superior and lateral surfaces of the temporal lobes?

Dr. K. S. Lashley, Orange Park, Fla.: Dr. Cobb has presented an interpretation of the relation of the mind to the brain which seems inevitable, in view of the complexity of psychological functions and the evidence on the functional specialization of cerebral areas. Mind has no distinguishing character except its organization. It is a complex pattern of interrelated activities which vary from moment to moment, yet are lawful and predictable in their relations. As we get more information concerning the interplay of neural events, it becomes evident that the organization of neural activity has the same characteristics as has the organization of mental events. The structures or patterns of the two are identical, and the mental events may be regarded as an indicator of the neurological processes, just as a reflex pattern is an indicator of the pattern of the neurological activity which produces it. The task of neurology is to discover the mechanism of this integration.

The activities of the brain at each moment are an integration of the activities of the preceding moment, plus some additional sensory input. The present moment thus has the characteristics of an awareness of the preceding moment; it is a continual integration and simplification of what has gone before. I have not time here to develop this "reaction theory" of mind. I published a detailed statement of it (*Psychol. Rev.* **30**:237-272; 329-353, 1923), in which I tried to show how such an interpretation can deal with such questions as the focus and fringe of attention and with some of the pseudoproblems, such as sensory quality and transcendence of time, that philosophers have injected into the mind-body question.

Both Dr. Cobb and Dr. Penfield have stressed the importance of the problem of the temporal organization of behavior. This is, I think, the most fundamental and the most troublesome problem in neurology today. I believe that its solution may be found by studying the translation of temporal orders of action into spatial patterns, and the reverse. It is possible to represent a short temporal sequence in terms of spatial dimensions, to manipulate those dimensions and, by scanning them in various ways, to retranslate them into another temporal pattern. Perhaps I can demonstrate this with Dr. Cobb's little melody. [Dr. Lashley whistled the tune as it was presented on the slide, then whistled it backward.] I think that what must happen in such a case is that the after-discharges of the sensory excitations persist with a spatial distribution in the brain, which can be scanned by some other mechanism.

I am less impressed with the analogies of various machines and neural activity, such as are discussed in "cybernetics." There has been a curious parallel in the histories of neurological theories and of paranoid delusional systems. In Mesmer's day the paranoic was persecuted by malicious animal magnetism; his successors, by galvanic shocks, by the telegraph, by radio, and by radar, keeping their delusional systems up-to-date with the latest fashions in physics. Descartes was impressed by the hydraulic figures in the royal gardens and developed a hydraulic theory of the action of the brain. We have since had telephone theories, electrical-field theories, and, now, theories based on the computing machines and automatic rudders. I suggest that we are more likely to find out how the brain works by studying the brain itself and the phenomena of behavior than by indulging in far-fetched physical analogies. The similarities in such comparisons are the product of an oversimplification of the problems of behavior.

Dr. Penfield's observations on the effects of stimulating the temporal lobe raise many problems, but I do not believe that they justify the conclusion that memories are stored

specifically in that region. He finds that removal of the excitable area does not destroy the memory which can be elicited from that area, and he explains this fact by assuming a bilateral localization. A bilateral temporal lobectomy in the monkey produces a badly deteriorated animal, who seems to have forgotten his previous training. But we find that training after operation on a new and different habit will restore his memory for similar habits, which he seemed to have lost. Thus, if the memory for differential reactions to a number of black and white visual forms or pictures seems to have been destroyed by lobotomy, and the monkey is trained after operation on the discrimination of red and green, this training produces spontaneous recovery of the other memories for uncolored forms. This is true for bilateral lesions of the temporal lobe; it is true also for bilateral lesions in any part of the posterior association areas. Such evidence seems conclusive that the memory traces are not stored exclusively in the temporal areas.

I have no clear alternative to offer in explanation of Dr. Penfield's data. The functions of the whole posterior association area are at present completely obscure. Bilateral destruction of the supposed visual association areas does not abolish visual memories, nor does destruction of the parietal areas abolish tactile memories in monkeys. Dr. Penfield considers that he is stimulating specific memory pathways. We do not know what cerebral processes arouse memories. It is quite possible that a memory trace is activated by a particular frequency in, or pattern of, reverberatory circuits. The memory itself represents a very complicated pattern of interacting processes. It is possible that pathological tissue in the temporal lobe may develop abnormal reverberatory circuits which chance to correspond to some elements in those of a widespread memory pattern, so that stimulation of the region activates only a specific memory.

The posterior association system seems to be a single functional unit, but the temporal lobes are the most important part of this system, a focal region for the most complex integrations. The defects following their removal in monkeys seem to be a difficulty in the comprehension of total situations, rather than a loss of specific elements of behavior.

Finally, I should like to speak a word of warning against the present tendency to ascribe very complex functions to the thalamus and brain stem. These are regions of relatively few cells and poorly developed internuncial systems. The lateral geniculate nucleus of the monkey, for example, contains only three neurons for each visual-acuity unit of the retina; that is, there are only three geniculocortical paths for each differential distance on the retina. Certainly, there is not in the lateral geniculate nucleus any large excess of cells which can serve for complex integrations. The same is true, I believe, for all other thalamic nuclei. The pulvinar of the monkey contains only 0.5% as many cells as does the parietotemporal region, to which its fibers project. In man the ratios of cortical to subcortical cells are certainly much greater.

It should be a fundamental principle of neural interpretation of psychological functions that the nervous activities are as complex as the psychological activities which they constitute. Consider, for example, the great numbers of motor cells that are involved in the pronunciation of a single word—the innervation of muscles of the chest, larynx, tongue, and jaw. The thought of the word is an internal pronunciation and can scarcely be produced by a smaller number of elements than is involved in the neural pattern which excites and controls the relative intensities of the motor discharges. The internal enunciation is a very small part of the total activity which must accompany it. Consider, for example, the number of meanings of the word "right" that are aroused when one hears the following sentence: "The millwright on my right thinks it right that some conventional rite should symbolize the right of every man to write as he pleases." The repeated pattern of sound, "right," is accompanied by a wealth of associated patterns, which must greatly exceed in complexity the auditory pattern excited by the sound.

I have emphasized here the tremendous complexity of memories, and I do not see how it is possible for the small number of cells in the centrencephalic system to mediate, or even transmit, these complexities. That system is anatomically very simple, and if it fulfills its function as a dynamic center, as Hess has called it, I think it will probably have exhausted all of its possibilities.

Dr. Abraham M. Rabiner, Brooklyn: Dr. Cobb stated that mind is a relationship. This symposium emphasizes that all cerebral activity is a relationship. It is obvious that no type of activity is initiated anywhere in the brain. Some impulse entering through the sensorium initiates activity. The clinician often observes findings that he cannot explain by previous

knowledge. He then speculates, and his thoughts are regarded as analogies. Bernardus Brouwer suggested that attention has as its anatomical basis corticothalamic as well as thalamocortical, interrelationships.

Dr. Jefferson Browder, by sectioning the anterior limb of the internal capsule in cases of parkinsonism, abolished tremor. In studying some of these cases, we noted that after operation the patient seemed unaware of the extremity which had been the site of tremor. For instance, he would sit on it; if he was asked to elevate his arms, he would lift the other arm, and not the affected extremity. When he was told to lift the arm affected, he did so. He had no disturbances of any types of sensation. It was obvious to us that here we had an illustration of Brouwer's concept that afferent and/or efferent fibers to the cortex had been sectioned and that the normal attention for the affected limb had thus been impaired.

Some years ago I presented a concept that all types of abnormal involuntary movement originate in the restless environment about us; that they enter through the sensorium but do not appear in our normal routine activities because they are interrupted, modulated, and changed by the basal ganglia; that when any of these nuclei are diseased, these movements which originate in the environment are then not altered and appear in the musculature as abnormal involuntary movements.

The program this morning constitutes a significant contribution to our knowledge, and gives to the clinician some support for what has heretofore been at times called analogy and speculation.

Dr. Henry A. Riley, New York: I think Dr. Merritt asked you, Dr. Penfield, whether there was any evocation of olfactory sensations. I did not remember any reference to the evocation of visual or somatic sensations in your stimulations. It seems to me that the stimuli were entirely limited, as I heard them, to auditory ones.

Dr. Emanuel D. Friedman, New York: One must agree that we have had an intellectual treat this morning. I was particularly pleased to hear Dr. Kubie discuss Dr. Penfield's paper, because some of us have felt that there has been too much divergence between the analytical school and those of us in clinical neurology. We hope that his statement of this morning is an augury of what we can look forward to, and we welcome him back into the fold.

No one, particularly a clinician, would dare to challenge Dr. Lashley's thesis of a residue of the equipotentiality of the cortex, even in man; yet, speaking particularly as a clinician, I would say that while there are disturbances in memory in cases of frontal-lobe lesions, as one sees them in some cases of brain tumor and arteriosclerosis, it is a clinical fact that the phenomenon which Dr. Penfield spoke of—very much allied to dejá vu—is particularly a symptom of temporal-lobe lesions; the voluminous dream states of Hughlings Jackson belong in the same category. May I cite, out of my own experience, two cases illustrating my point? One was a case of tumor of the temporal lobe with hemianopsia. At intervals the patient had convulsive episodes, which began with an aura of seeing an old woman in rags in the hemianoptic field. He later recalled that there was such a person in the town from which he came many years ago. The other case was that of a sea captain who also had a temporal-lobe tumor with convulsive seizures, at the onset of which he had a gustatory aura, consisting of the tasting of Jamaica rum. I feel, therefore, that the particular type of memory phenomena which Dr. Penfield described has its origin in the temporal lobe.

Dr. Stanley Cobb, Boston: I should like to ask Dr. Penfield whether it is only in epileptic patients that he is able to elicit these memories and, if so, does he have an explanation therefor?

Dr. Wilder Penfield, Montreal, Canada: Dr. Merritt and Dr. Riley brought up interesting points.

Dr. Merritt suggested he would expect olfactory memories to be recorded in the temporal cortex. He pointed out that smells bring back memories. We have stimulated the region of the uncus and the hippocampus almost as frequently as we have the convexity of the temporal lobe, because often the epileptogenic focus is in the uncus and hippocampus and runs along the incisura temporalis. No one has yet said that stimulation has caused him to remember a smell. In ordinary life, odors may bring back an elaborate memory. It is not the memory of an odor that is brought back.

Dr. Riley noted that I did not refer to somatic memories. There have been none, unless one considers that the apparent displacement of the body into another neighborhood constitutes a somatic sensation.

Dr. Lashley pointed out, as I feared that he would, that in his opinion there are no specific memory traces. That is in keeping with his observations in the early days in Minneapolis, when he worked with rats. It is in keeping with his demonstration of the replaceability of areas of brain, functional areas of brain, one by the other. Yet if there are no recording patterns in the cortex, how is it that an electrical stimulus can cause the patient to reexperience an earlier experience?

I would point out that the replaceability seems to be somewhat less as one rises in the evolutionary scale. Memory patterns may be duplicated in the two temporal lobes. The memory areas may extend into parietal cortex, but they do not seem to extend under the temporal lobe all the way to the hippocampus.

Dr. Cobb brought up the question as to whether this induced recollection has occurred only in epileptic patients. The answer is "yes." I do not know, of course, that such recollections cannot be produced in normal persons. We do not stimulate the cortex of normal subjects. I can say that when the local cortical seizure or local cortical focus is in, for example, the central area or a frontal area, we have never had memory responses from the temporal region. We get them when the focus is in the general temporal area or close to it, as in the occipital area, which borders it.

Certainly, it is clear that the effect of local epileptic discharges is to facilitate the cortex for response to the electrode. That is not only limited to memory. The same is true of other areas of the cortex. It seems to be true that one cannot force an area of cortex to respond by increasing the strength of stimulation; at least, we never have. We keep our strength of stimulation down. If we push the strength up, we may produce a seizure, but we do not force out a memory, if the cortex is not ready to give it. The cortex seems to yield what it is ready to give. That is true also of the sensory areas, the somatic sensory, and the visual.

Often, in stimulating the visual cortex, we have been surprised not to be able to produce a visual sensation. Possibly even stronger currents might be effective, but I have hesitated to use them.

Dr. Cobb has given us an extraordinary broad survey of mind and brain relationships. I like his statement that the mind depends on the integration of one functional part of the brain with another.

I do not consider valid Dr. Lashley's objection that the centrencephalic system is too small to do what we want it to do. He seems to think that we assume that the centrencephalic system is a sort of a room by itself that does all these things. The system does not function by itself. It functions together with all the other areas—cortex and other parts of the central nervous system. Thus, when it is functioning, all parts of the brain that are needed for that particular function come into action.

Special Article

CONSCIOUSNESS RECONSIDERED

FRANCIS SCHILLER, M.D.
SAN FRANCISCO

CONTENTS

INTRODUCTION

THIS PAPER is an attempt to bring some order into the various problems which are raised whenever that loose and elusive word "consciousness" is used. In trying to clear my own mind, I am also indulging in the hope of preparing some common ground on which the philosopher may meet the physiologist. Common ground should imply common sense, and may not exclude the commonplace.

Multiplicity of Meanings.—If it is true that science is a language, it is also true that a language cannot do without metaphors and models. Science often expresses one set of human experiences in the terms of another set, as, for instance, when the physicist speaks of "waves," the histologist of "tissues," and the psychologist of "perception" or "grasping." Explanations are accepted or rejected according to how appropriate a set of metaphors is felt to be. This fact makes an inescapable necessity of Aristotle's μετάβασις εἰς ἄλλο γένος ("the transgression into another field [or kind]"), which he deplored; but a feeling of appropriateness also determines the limits to which transgression may be practiced without giving offense.

We are therefore concerned with the definition of a term, as well as with a hypothesis as to how that which is to be defined may work.

From the Division of Neurology, University of California School of Medicine.

It is likely that any group discussing our subject matter—which one might call "neurosophical"—will wholeheartedly agree only on one point, namely, that consciousness has various meanings in various contexts. Miller,[1] in a monograph on "Unconsciousness," has collected 16 of them. His list, shortened and applied to our subject, yields the following, partly overlapping, items: (1) responsive to stimulation, i. e., awake and alive; (2) sensing, i. e., with sensory pathways conveying stimuli; (3) attending, noticing; (4) having insight and discrimination; (5) remembering; (6) being able—and willing—to communicate, and (7) acting voluntarily, as well as the (8) psychoanalytic meaning.

Subjective and Objective Aspects.—The study of consciousness may, however, be directed by two main trends:

I. The subjective,[2] or direct, inquiry. This is concerned with the constituents or contents of consciousness, such as the self, thoughts, images, percepts, and feelings. Its field is what we are conscious of, and has been cultivated by philosophers and most psychologists. Its main method is introspection.

II. The objective, or indirect, inquiry into the behavior of others, both human and animal—in other words, the question of what is a conscious, as opposed to an unconscious, organism. Its methods are those of the biological sciences.

The division into a subjective and an objective aspect of consciousness is evident in Gowers'[3] classic "Manual":

> The terms "conscious and consciousness" are, however, used in two senses: first to signify the subjective knowledge of the occurrence of mental processes; secondly, to designate the outward manifestations of such processes. In medical language the term is chiefly employed in the latter sense. A patient is said to be "unconscious," or to have "lost consciousness," when there is no spontaneous evidence of mental action, and none can be elicited by sensory stimulation. Hence the term "insensible" is often used in the same manner. Another confusion is introduced by the frequent relative use of the word "conscious of" in the sense of cognition or knowing. Thus the delirious patient may be said to be unconscious of what is occurring around him, although he is not said to be unconscious.

To us the phrase "to be 'conscious of' in the sense of cognition" seems synonymous with "subjective knowledge." And the delirious patient, though not "unconscious," must be considered as being in an abnormal state of consciousness, regardless of whether we take "abnormal" as a matter of degree or kind.

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1. Miller, J. G.: Unconsciousness, 1942, New York, John Wiley & Sons, Inc., 1942, pp. 22-43.

2. It will become clear in the course of the discussion that the term "subjective inquiry" is somewhat paradoxical in this context, and that it has been used only for the sake of convenience. It denotes the method of inquiry, rather than any metaphysical premise. In clinical usage, for instance, "subjective" is an attribute of "symptoms," as opposed to "signs," which are spoken of as "objective." Obviously, the line between subjective and objective, or symptoms and signs, is difficult to draw. But let us agree that inquiries deal with objects and must therefore be objective. Moreover, I hope to show that the contents of consciousness, i. e., what we are conscious of—and with this the self will have to be included—can largely be reduced to objects.

3. Gowers, W. R., and Taylor, J.: A Manual of Diseases of the Nervous System, Ed. 2, London, J. & A. Churchill, Ltd., 1893, Vol. I, p. 99.

The same unresolved dilemma between the objective and the subjective recognition of consciousness is inherent in Penfield and Erickson's [4] discussion of epileptic automatism:

> . . . A man may be said to be normally conscious when he gives evidence that he is aware of his personal environment, understands his own purposes in a manner which the observer considers to be normal for him.

Objective signs are obviously not deemed sufficient for an unequivocal diagnosis, for whatever in this connection "giving evidence" may mean, we read of the necessary taking into account of subjective symptoms, i. e., of what the man tells us. The authors go on to say:

> . . . Thus activity is an evidence of consciousness in an individual only when it indicates awareness or understanding of the significance of his own acts and experience. Consciousness, therefore, may be considered as the state of being aware of one's own thought and purposes.

In other words, what practical evidence we have is derived both from behavior, which is objectively demonstrable, and from the faith we put into a man's subjective utterings. His own retrospective memory becomes an invaluable guide for establishing whether someone has been conscious at any given time. Not an infallible guide, however, for events happening to a conscious person may be blotted out for subsequent recall in retrograde amnesia and simple forgetting.

THE SUBJECTIVE INQUIRY

Clearly, an extensive discussion of how consciousness is experienced by the conscious subject revives many age-old epistemological and psychological controversies, which are beyond both the training of a neurologist and the limits of this paper. To express some personal views on these matters has, however, seemed inevitable. These views [5] may well appear sketchy and flippant, and they are presented with due apologies.

Development of the Ego.—What is the Ego? Who is the Self turning around itself? How can a subject deal with an object which is its own identity, and infer, with Descartes, its own existence from its own thinking?

The Self as an Object and an Objective.—"I am the man I'm looking for," insistently repeated the singing comedian Vic Oliver; was he thus taking off the absurdity of our subject matter, as well as that of old opera? Are we not here the dupes of a conspiracy between grammar and metaphysics?

Let us try the biological approach. Taking one of our phagocytes, we find that it is part of our self, but in all other respects similar to an ameba, which is its own master. Nor have we any more conscious control over the greater part of our body than over the phagocyte. Now, this cell may be chemically attracted to a microorganism and eventually engulf it. We shall not need to quarrel about calling our phagocyte a living entity, reacting to appropriate stimuli with a good deal of discrimination and, maybe, with a purpose. It is a matter of literary taste, not of logic

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4. Penfield, W., and Erickson, T. C.: Epilepsy and Cerebral Localization: A Study of the Mechanism, Treatment and Prevention of Epileptic Seizures, Springfield, Ill., Charles C Thomas, Publisher, 1941, pp. 143, 144.

5. Views, that is, on the ego; on memory, reason, emotion, and will; on direct and indirect experience; on parts and wholes, abstract and concrete.

or evidence, whether or not we call an ameba, a phagocyte, or even a germinal cell *hungry*. If we do not, it is because these organisms, or relatively independent parts of organisms, are in so many other ways dissimilar to ourselves that we prefer to reserve a word like "hungry" to somewhat more complex organic structures. Thus, we do say, not of a fetus, but of a baby, that it is hungry.

When the child's reactions become more manifold, when excitation and inhibition weave a more subtle pattern of response, when crying has been replaced by the articulate asking for food and its intake is more mannered, then we are tempted and, I think, allowed to say: The child is *aware* of being hungry. It has acquired such wealth of coordinated means to perceive and react that we begin to call it conscious of its surroundings. In the child's vocabulary, there are soon words for objects referring to needs and to a subtler form of needs—interests. Later another object is differentiated out and its name taken over from the speech habits of the child's attendants; this is the child's own name. Probably later still the child refers to itself as "Me."[6] Our small child, as time goes by, becomes aware not only of the fact that it is *hungry*, but that *it* is hungry. It finds out that there is a deeper meaning attached to the little, no, the big, word "I," by which everyone around designates a different person. Such introspection, though prepared gradually, may be of an explosive, revelatory character. In some people's lives this revelation may not be greater than the emotional stir produced by the sudden insight into a mathematical problem, but it nevertheless is made dramatic by being launched with a good deal of affective energy.

Inseparable from the child's discovery of its own self is a change in its outward relations. It gains insight into the fact that it has become an object for the perception and judgment of others. This seeing oneself through the eyes of others, in other words, the development of embarrassed "self-consciousness," has great emotional implications, which are much stressed by existentialists, and contribute much to our behavior in society. Some psychoanalysts will call it the superego, and everyone understands it by the word "conscience." Something like observable egoism, of course, has been displayed by the child ever since it was a fertilized ovum —if we want to start its career at this arbitrary point. The discovery of the self as an objective of the organism's zest for life has merely added subtlety, poignancy, complexity, and versatility to its former skill in coping with the environment. At the same time, egoism has been infused with awareness of social values. The new *object*, the ego or personality, turns out to be the symbolical image and personification, the conceptual abstract of the body and all those energies which have been at work ever since birth. In fact, they have been active since as far back as one wants to go. This concept is therefore endowed with all the organism's drives and fears. As a person grows up from a unicellular structure, he retains some properties of that structure, but he also develops more and more complex intercellular relations, thus becoming, as well as being at each instant, a new integrated whole. Ego-awareness, self-consciousness, or, as Koffka calls it, "ego-segregation," is a relatively late

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6. This form of referring to the self as to an object has persisted in English usage in moments of emphasis ("What, me?" or "It's me!"); the French also use their objective *moi* for the first person singular. The pronoun "ego" and its equivalents appear as such only for emphatic purposes in Latin, Greek, Italian, and the Slavonic and other languages; personal activity, in these languages at least, seems not to be regarded as necessitating special reference to an introspective ego.

acquisition, inseparable from the steps of biological growth and from the ever-changing part it plays in daily life. "To be conscious of one's self is only a correlate to being conscious of objects" (Goldstein [7]).

Yet we still have to account for the grammatical and logical difficulty that "I know myself," i. e., that in one and the same proposition subject and object are identical. As soon as I ask "Who am, or is I?" in this game of dog chasing its own tail, I am caught in a closed circle, or, worse, I am trying to make a point point to itself. Thought as an activity clearly must be directed away from its starting point. I have to set up a concept of myself in order to deal with it. "I" cannot have any meaning unless some mental content is projected somewhere in space and time. The conceiving of an ego is probably as close as we can come to absolute "here" and "now"; in fact, these two terms get their only meaning from an egocentric concept. Yet all three do not satisfactorily emerge in any attempt at realizing them unless they are set off against their neighboring opposites, i. e., their environment, against "they," "there," and "then."

We have seen that the self and consciousness are developed both in a phylogenetic sense—from the ameba to man—and in an ontogenetic sense—from the ovum to the adult. This was their biological history. But in a logical sense, too, every single statement about the ego must have its predicative antecedents to endow the word with meaning. The phrase "I am hungry" entails knowledge of the subject "I" derived from previous experience; before becoming a subject, it must have been the object of a thought. Every statement, be it about the ego or any other subject, is based on a precedent which is tacitly, and often unwittingly, taken for granted. The "I" of any sentence is a projection out of the organization of my body, but it remains attached to it, as the moving picture on the screen is linked with projector and film. Both have their seeds, their antecedents in the past, their pointers to the future, and their connections in space.

If the concept of ourselves, though contracted into the rigid single word "I," is an abstract notion of vast, vague, and varying outlines, we nevertheless feel the animal energy by which the ego is driven and the social responsibilities by which its conscience is guided. What have been amorphous feelings of pleasure and displeasure, affirmation and denial—so called in retrospect and translated into adult language—coalesce with the moral value-judgments of good and bad.

The plan which we may construct of our organization cannot be called an entity residing "inside" ourselves. The knowledge of the ego boils down to the fact that among any and all of the real and imaginary objects known to a person there is one which may be called "the knower," and he often takes precedence. Summarized, the ego is, biologically speaking, the way an organism has of integrating its past history and future aims with its present structure and relations to the environment. Logically, it is a time-saving summary and abstract; a "pointer-word" or "label" (Eddington [8]) which stands for the unity of consciousness; "a logical fiction, like mathematical points and instants . . . introduced not because observation reveals

7. Goldstein, K.: The Organism: A Holistic Approach to Biology Derived from Pathological Data in Man, New York, American Book Company, 1939.

8. Eddington, A.: The Philosophy of Physical Science, New York, Cambridge University Press, 1939, pp. 110, 123.

it, but because it is linguistically convenient and apparently demanded by grammar" (Russell [9]).[10]

Having thus followed the development of the first person singular from its humble beginnings, that is, from a stage so undifferentiated that it was unaware not only of itself but even of its surroundings, we may argue that unconsciousness is the ancestor and source of consciousness. This ancestry pertains to the development of the species, the development of each individual member of the species, and to each instant of a conscious organism.

Psychoanalytical Notions.—At this point it is impossible to by-pass Freud's great contribution of having emphasized and analyzed that larger part of ourselves which is unconscious; at the same time, it has appeared to many that a too rigid adherence to psychoanalytical doctrine may be a hindrance to progressive understanding. In the ego and the id (Freud [11]), on the one hand, and "the conscious" and "the unconscious," on the other, we have two overlapping frameworks and sets of reference, conceived anatomically, as well as functionally. The ego is a "cortical homunculus" and contains conscious, as well as unconscious, processes. These are spoken of as mental units which—apart from being subject to condensation and distortion—remain fit to move in and out or stay imprisoned in certain parts of the brain. The cortex is apparently reserved for the conscious parts of the ego; the basal ganglia and brain stem, for what is unconscious in the ego and for the id. Percepts are envisaged as conscious "from the start"; images, as "a very incomplete form of becoming conscious"; ideas "need the connecting link of verbal images to become conscious," but feelings are in no such need.

The general objection to this theory is that it unwittingly and indiscriminately ascribes consciousness and its opposite both to mental elements, such as ideas and feelings, and to the structures which contain them, such as the ego and the id. Both the containers and the contained are believed to be charged with energy, and our imagination is stimulated, as well as critically roused, by all these dramatic happenings between conspiring, disguised, rebellious animalcules and their oppressors, jailers, and prison walls. There is no distinction between similarity and identity, no differentiation of strange metaphor, intrinsic process, and outward manifestation. It is not clear whether and how the unconscious differs from the merely physiological, on the one hand, and from the unknown or ignored, on the other. A recent step in the necessary development of Freudian notions has been made by Rado.[12] He characterizes unconscious mind as "an extrapolated concept rather than a thing in itself" and identifies unconscious with physiological events. A so-called "uncon-

9. Russell, B.: The Analysis of Mind, London, The Macmillan Company, 1921, pp. 141, 230, 307.

10. It is only in theory that we can dispose of the "subject" and reduce it to one or many objects, insisting that all inquiring must be objective, that is, into something. In practice, however, "I" or any other "subject" serves as an ordering principle, a set of coordinates, as it were. Or we might call it the unprecedented and indivisible One, put at whatever moment and place we start—the crystallizing or rallying point for every proposition. Without the practical assumption of a first stroke, there would be chaos, the infinite and infinitely divisible, amorphous chaos of antecedents which reigns before any—arbitrary—beginning is being made.

11. Freud, S.: The Ego and the Id, London, Hogarth Press, Ltd., 1927, p. 9.

12. Rado, S.: Mind, Unconscious Mind, and Brain, Psychosom. Med. **11**:165-168, 1949.

scious desire," for instance, is interpreted as merely a way of referring to a causal agent which is "nonreporting" as far as consciousness is concerned.[13]

Organisms, Not Processes, Are Conscious.—Thus, in order to avoid confusion, we have to decide whether to apply the term "conscious" to an organism or to mental processes. This may seem like splitting hairs, for is an organism not the totality of its processes? Such processes, however, are hardly open to subjective introspection; only when they are transformed into concepts, can we become aware of them with any degree of certainty. We cannot conceive of them in the animistic fashion of psychoanalysis. As processes, they must be lively enough; dynamic, but not alert; not aware of themselves or of anything else. It seems, therefore, that we should not call "conscious" the feelings and thoughts, percepts and images, but should so designate only the state of the organism in which they occur. Thought means two things; one is the private unconscious, or physiological (von Kries[14]), process which nature performs in us; the other is its public product or content, a symbolic object for introspection or verbal communication. To quote James[15]:

> Whilst alive they [the mental states] are their own property, it is only *post-mortem* that they become his (the psychologist's) prey. . . . Each thought is born an owner and disowned. . . . Nothing can be known *about* till it be dead and gone . . . The *effective* consciousness we have of our states is the after-consciousness.

Brain[16] stressed this time lag inherent even in perception:

> We are always anything from a fraction of a second to a few thousand years (in the case of perceiving the stars) behind the times.

Memory.—Introspection therefore deals with memories only, be they ever so recent, and consequently posing as speciously present events. "A memory" is an unconscious past event of the mind; when it is in the process of reactivation, we may become conscious of it, that is, when it is incorporated into a larger field of mental activity.

Now memory, or learning, taken in its broadest sense, has been considered as a universal function of organized matter (Hering,[17] Samuel Butler,[18] Semon[19]). One may go so far as to ascribe memory to all events recurring in nature, or one may reserve the term for the habits of living organisms only, or, finally, one may restrict it to acts of remembering in conscious higher animals, especially men. The limits to ascribing memory to anything alive are, if possible, even wider than those regarding consciousness, but they are equally arbitrary. When a term is stretched by one school to the point of embracing too much, another is sure to taboo that term

13. "Dianetics," an unprofessed Freudian heresy promulgated by Hubbard (Hubbard, L. R.: Dianetics: The Modern Science of Mental Health; A Handbook of Dianetic Therapy, New York, Hermitage Press, 1950), dealing, in a rich jargon, with engrams, consciousness, and the ego, belongs to the realm of science-fiction.

14. von Kries, J.: Allgemeine Sinnesphysiologie, Leipzig, F. C. W. Vogel, 1923, p. 294.

15. James, W.: The Principles of Psychology (1890), New York, Henry Holt & Company, Inc., 1910, Vol. 1, pp. 139, 165, 189, 339, 644; Vol. 2, p. 82.

16. Brain, W. R.: The Neurological Approach to Perception, Philosophy **21**:134-146, 1946.

17. Hering, H. E.: On Memory as a Universal Function of Organized Matter (1870): cited by Butler, S.: Unconscious Memory (1887), London, Jonathan Cape, 1922, pp. 63-86.

18. Butler, S.: Unconscious Memory (1887), London, Jonathan Cape, 1922.

19. Semon, R.: The Mneme, London, George Allen & Unwin, Ltd., 1921.

as unfruitful or meaningless, while a third will try to keep or reintroduce it in a limited sense. At any rate, some form of memory enters into every activity of a conscious mind. It does so in particular when we recollect and use past experience in acting or in planning the future. Now, the objects succeeding each other in the mind may be called events, and when they survive in any recognizable form, memories.

Bertrand Russell [20] defines "event" "as a complete bundle of compresent qualities, i. e., a bundle having the two properties "(*a*) that all the qualities in the bundle are compresent, and (*b*) that nothing outside the bundle is compresent with every member of the bundle." [21] Russell also distinguishes between a "physical" event, which is inferred, and a "mental" event, "with which someone is acquainted otherwise than by inference."

Direct and Indirect Experience.—In these statements we are confronted with two fundamental problems concerning the analysis of consciousness. One is that of parts and wholes, or of isolated qualities and bundles of qualities; the other, the problem of direct and indirect experience. Let us take the second problem first.

It seems that too much stress has been laid on the uniqueness of "direct experience." Between direct, or sentient, and indirect, or sapient, experience there is a continuous line, rather than a break in meaning. Direct experience is only an incomplete form, the raw material as it were, of the indirect. At one end of that line we may put the unconscious, physicochemical passing on of the stimulus; at the other end, reflective and verbalized thought. Between these two extremes are sensation, perception, and image formation, as classes of increasingly complex organization. Direct data are private; but they can be, and frequently are, elaborated into indirect, or public, ones. Whenever this happens, we speak of "knowledge." Knowledge, if communicable, is never quite direct; it implies inference. What distinguishes direct from indirect experience is merely the degree or strength of inherent immediate belief, which is higher in the direct form. For example, I alone can become conscious and most thoroughly convinced of a bodily sensation, such as a certain pain. But my knowing of that pain requires some elaboration. As a human experience it acquires a name; it is attached to other experiences and so becomes indirect. It participates in public experience. Nor is there a fundamental difference between this sensory experience and the publicly verifiable experiences of the other senses. These can also be arranged in a line of progressive complexity and precision. The most critical, the best controlled and public-spirited, as well as the least passive, of the senses is vision. What, on the most private end of the scale, we call "feelings," are vague, but most convincing, indeed compelling, experiences referable to a mixed autonomic and somatic, but mainly autonomic, origin. Even if we have to reject the full implications of the James-Lange theory regarding the purely peripheral origin of the emotions, there is no doubt that autonomic and sensorimotor, as well as some

20. Russell, B.: Human Knowledge: Its Scope and Limits, London, George Allen and Unwin, Ltd., 1948, pp. 245, 312.

21. In other words, the definition stresses both the element of coherence an event has and that certain degree of discontinuity which singles it out from all other events that surround it in space and time.

"mental," characteristics are intimately blended in those feelings which are most private. Our reactions to them are relatively potent; our introspection into them is relative impotent. But what introspective elaboration, what accuracy of verbal expression, we can lend them renders such primitive mental events appreciably public and puts them into the realm of inference. It is true that sensations of pain, of smell, and of taste cannot be made as precise and public as positional and visual impressions. The latter are the exquisite carriers of analysis and synthesis, the groundwork on which our systems of symbols for public use are erected. Descended from them in another line are also our measuring and amplifying instruments, which enable direct experience to become indirect and scientific. Although precise and subtly organized, the percepts and concepts derived from vision carry a smaller degree of immediate and uncritical belief than painful sensations do; the former are not only capable, but demanding, of some public confirmation.

It might be objected that thoughts, however elaborate, are private events and objects of direct experience. It is true that they cannot be inspected by others in the way in which public sense data, or, rather, their objective origin in the environment, can. But it may be conceded that both to think and to experience thought is bound up with our language, logic, and social environment, all of which are eminently public. A thought is certainly a mental event, but we cannot "be acquainted with it otherwise than by inference." Thus, any mental event, as soon as it has ceased to be so utterly vague a feeling that we "know" about it, loses some of the character of directness, a character which can safely and fully be ascribed only to innate reflexes. Mentality or knowledge is the acquired result of learning.

Parts and Wholes.—The other fundamental issue to be considered is that between parts and wholes. The fact that we know of the existence of any event implies that we have appreciated it as a coherent unit, a particular whole, and drawn some inferences in relation to it. An event, be it mental or physical, imaginary or real, owes its existence to some coherence and continuity, in space and time, of its parts or qualities. For "existence" we may substitute "identity." This continuity applies to an organism, as well as to a nervous system, to consciousness, and to its objects. But the notion of such continuity has to be qualified, for a whole, though coherent and isolated, is surrounded by background forces in space and time, which are necessary to bring it into relief. To define a whole, we have to take into account what it is not, as well as what it is. These extrinsic forces influence it in many ways, to the extent of jeopardizing its identity. Indeed, the longer it exists, the more doubtful its identity becomes, being altered by forces affecting it both from within and from without. It has to be added that by "parts" only those qualities which are relevant should be understood, for in any mental event there is involved relevance, a judgment of relative value.

Analysis and Synthesis, Abstract and Concrete.—As well as analyzing, the mind is unifying everything within its compass. Analysis and synthesis seem to alternate constantly. When we switch from the whole to the detail, from the bundle to the single quality, it is this single quality which we instantly convert into a whole as we focus our attention on it. Meanwhile, the original greater whole, the bundle, has been neglected as a mere background; our former attitude

to it may, nevertheless, be resumed at any subsequent moment. Similarly, we may move on to the abstract part-whole relationship and embrace it as our present whole.

Such wholes, "one thing at a time," are rapid abstractions, consisting of a limited number of qualities which have been taken from the physical event or stimulus. Thus, abstraction, or generalization in its widest sense, no less than memory, is a basic biological function, as was also postulated by Semon,[19] Lashley,[22] and Korzybski.[23] (We cannot remember without generalizing, and cannot generalize without remembering.) Our sense receptors are called analyzers, because each of them can abstract only one quality from any concrete physical event. None of the analyzers, however, normally works in isolation; their work as a team is synthetic. One might say that their work is analytic so far as the event is concerned, but synthetic in view of the organism. Yet this distinction is blurred by the fact that we experience the event as a whole, and not really as a "bundle of qualities"; and we do so either by inference or because of its Gestalt. The processes of analysis and synthesis, perhaps owing to the speed with which they occur, are therefore difficult to keep distinct. And so are our notions of the concrete and the abstract, the particular and the universal. That these are blurred has been pointed out by Whitehead.[24]

Mind and Matter.—Of course, we are far from a satisfactory common basis for mental and physical events. Those who employ the controlled conditions of the laboratory are used to seeing the bundles of physical events neatly split up into their components, such as wave lengths and atoms; these units are sufficiently distinct for a suitable arrangement on the left side of an equation, and are shown to equal the whole event, standing on the right. For mental events such a procedure has so far been impossible. All we know about isolated units in this field is that physiological methods will trace unconscious "messages" of a bioelectrical, and maybe chemical, nature. These methods, however, are silent about the next stage of organization, leading to the mental event. Nor have psychologists developed either a method or a terminology to apprehend parts or units of the mental complex. It is true that even into the physicist's concept of matter, into the laws of nature, the principle of uncertainty or indeterminacy had to be introduced; that for Russell[9] "mind and matter alike are logical constructions" and "the physical world is infected through and through with subjectivity"; that Eddington[8] spoke of the "impress of our frame of thought on the knowledge [of the physical world] forced into that frame" and of the "concept of substance" having "disappeared from fundamental physics; what we ultimately come down to is form." James[25] had already written that "thoughts in the concrete are made of the same stuff

22. Lashley, K. S.: Brain Mechanisms and Intelligence: A Quantitative Study of Injuries to the Brain, Chicago, Chicago University Press, 1929, p. 158.

23. Korzybski, A.: Science and Sanity: An Introduction to Non-Aristotelian Systems and General Semantics, Ed. 2, Lancaster, Pa., Science Press Printing Company, 1941.

24. Whitehead, A. N.: Process and Reality: An Essay in Cosmology, Gifford Lectures Delivered in the University of Edinburgh During the Session 1927-1928, New York, Cambridge University Press, 1929, pp. 66, 304.

25. James, W.: Essays in Radical Empiricism, New York, Longmans, Green & Company, 1912, pp. 3, 4, 37.

as things are," and Holt[26] maintained that there was a fundamental, logico-mathematical, "neutral stuff," common to mind and matter, and that the "neutral cross-section" of the two constituted consciousness. The generosity of physicists such as Eddington in giving unto the philosopher and the psychologist what is theirs, and perhaps even more, may mean only that any investigation driven far enough will land us in abstracts and in subjectivity, whether its subject be matter or mind.

Let us sum up our position. Among examples of the close interaction of objects in nature, that of living organisms and their environment is one of special complexity. We are baffled by the number of factors which our studies reveal. Observation hints that there is a device which the most complex of these organisms uses; this is loosely called mind, or thought, or consciousness, i. e., an efficient way of rapid analysis and synthesis. Mind, in other words, is a logical construction used to signify our ability to construct logically; hence, its elusiveness. We infer or postulate "mind" where the complexity of organization goes beyond the immediately observable and where we, nevertheless, have evidence of an agency which is effective, as well as capable of being affected.

The body-mind problem may, after all, be reduced to a question of linguistics. The relation between the brain and the mind is that between structure (in the anatomical, not the logical sense) and function, that is, in the last instance, between noun, denoting object, and verb, denoting action. The day will come perhaps when we shall be able to express all structure in terms of function and all things in terms of activity, but by then our thought and language will be so "dynamic" as to be unrecognizable from our midtwentieth-century point of view. So far, we may say that brain cells—nouns—are structure; their activity or function, what they do, is "to mind." This does not mean that the brain, as has naïvely been said, "secretes thought as the liver secretes bile." Yet the relation of structure to function is essentially the same whether we speak of the liver or of any other active entity, including the brain. The function of the liver is "to secrete," or secreting. "Secreting" is indeed something like thinking in the sense that it cannot be found or demonstrated as such; that is, it cannot be touched or weighed or divided into bits, to whatever mechanical procedure the gland is subjected. It can be found no more than "movement," which, like mind, is also a verb disguised as a noun, i. e., not a material, concrete thing, but a way of using the verb "to move." It can be measured only in terms of time. "Movement," "energy," are words used in physics. They express that immaterial state of change, in the fourth dimension, which is interdependent with and unthinkable without the assumption of solid, permanent things, things three-dimensional that can move or be moved, change or be changed.

"Bile," as opposed to "secretion," is indeed found; but bile is not the activity of the liver; it is a product of that activity. The brain, in its devious ways, also produces such objects, or has such late effects, e. g., metabolic products, electro-potentials, audible speech, or a readable book. But it is the way the brain does it —the doing, and not the result, or some added epiphenomenon—which is called

26. Holt, E. B.: The Concept of Consciousness. New York, The Macmillan Company, 1914, p. 182.

mind. As a verb, or a verb disguised as a noun, the doing, naturally, is immaterial. Mind is a word which stands, not for a thing, but for an activity, process, or function. Function is a linguistic or logical link between a causal thing and an effected thing. "Function" is as puzzling as "mind," which latter is an instance of it. "The dog barks"—the dog is a thing; "barks" is a linguistic help (or obstacle!) to express the fact that some physical sounds, which can be heard and recorded, are connected with the dog as effect is with cause. The nexus, or function, is expressed by the verb "barks." The "barking," the doing of the dog, cannot be found, only its result can, i. e., the material change produced on the acoustic apparatus of a listener or on a record.

Doing, verbs, functions, predicates, are in language as intimately fused with subject and object, or cause and effect, as is the marriage of time with space, or the fourth dimension with the three others from which it is so greatly different. Verbs are transitive or intransitive, or both, but these characteristics are more or less accidental. "The dog barks"—the intransitive form masks the essential character of the verb of linking subject to object, cause to effect. Without altering the meaning, "the dog does the barking," or, clearer still, "the dog makes barking sounds," restores the true relationship by the substitution of the transitive verb "makes." Taken out of their context, in their "ideal," infinitive form, all verbs can be looked upon as intransitive; in a context they can all, with proper treatment, be replaced by transitive ones. "A man walks" can be translated into "a man moves his limbs in locomotion"—clumsy but correct. "A man thinks" implies cause and effect. The cause is the man's brain and its past or present input; the material results are such as an electroencephalographic tracing, a poem written on a page, an apple displaced and eaten, or a mountain moved. But the thinking, the thought, the mind, is immaterial, because it is an abstract concept, a convenient temporal link between spatial, physical things. The fallacy lies in trying to give "ideas" a different status from that which they have, in a tendency to endow them, despite all evidence and common sense, with some self-sufficient corporeal or "ethereal" existence.

Magnitude and Indeterminacy.—It may be of help here briefly to consider the two factors of indeterminacy and of magnitude. Let us assume that life, based on the large protein molecules of the cell, is the most complex form or activity of matter, and mind, the most complex form or activity of organic structure, capable both of mirroring and of altering matter. We then, perhaps, need not be surprised that if there obtains a certain degree of indeterminacy for inanimate matter, a greater degree must be postulated for the organic world, and still less predictability, with a good deal of freedom, for the "molar behavior" (Todman [27]) of organisms guided by nervous systems. If the methods employed in nuclear physics are said to influence the single particle so that not both its speed and location can be identified, how much more uncertainty must be inherent in experiments on living organisms and mental functions, where a host of frequently unknown factors, unduly present or absent, and of doubtful relevance, may influence the results. Far more frustrating to the experimenter in psychology than in physics

27. Todman, E. C.: Purposive Behaviour in Animals and Men, New York, Century Company, 1932.

and chemistry are the conditions in psychophysiology, where infinitely larger "molecules," or more complex "molar" structures, where entirely hypothetical and undefined units of behavior defy analysis. Both in physics and in psychology the nature of the components is not directly apprehended but is inferred, either from their effects or from their origin. About mental events, however, we know nothing except their very remote origins and effects; and their composition, causation, and "biographies" seem to be inseparable.

Contrary to Bergson's [28] main thesis, we have no particular intuitive, or direct, and at the same time communicable, knowledge of our consciousness. Rather, we have to make a slight, but intellectual, effort in order to be aware that we have been, and shall be, conscious. Whether it is this fact or any other item of thought, we are always dealing with a complex that appears to us as a whole. It is of such wholes, singled out from the unbroken and vague background of temporal succession and spatial contiguity, that we are clearly conscious; these we call ideas and things, movements, and events. It is by "calling," that is, by fusing, them with personal or class names that we lend them stability and publicity.

Memory, Reasoning, Emotion, and Will.—Herbert Spencer and Hughlings Jackson saw consciousness as divided into memory, reasoning, emotion, and will, but realized that these were all involved together in conscious adjustment (Jackson [29]). How arbitrary the distinction is emerges from the consideration that these functions are largely expressible in terms of each other. Various schools of thought, all with a good deal of success, have claimed precedence for one such pseudoentity over the other, in an attempt at reducing the welter of mental factors to one or two basic ones. We have dealt with the universality of memory or learning, and with the presence, even at primitive levels, of reasoning, that is, the ability to generalize. We are also familiar with the contention that instincts and emotions are the primordial energy which drives behavior, and with the view that affective conflict leads to reasoning and consciousness. All such theories are deterministic. Wholesale determinism in science, however, has been somewhat limited by the overruling importance of statistical probability, the laws of chance diminishing the scope of both blind law and blind chance. We have rejected the extreme dualistic belief in a separate, semidivine ego as the arbiter of behavior, for its assumption is unnecessary and unwarranted and leads to an infinite regress.

After discussing the various aspects of "awareness," we still have to account for the traditional role of "will," or that essential aspect of consciousness which is said to control voluntary action. "Conscious" and "voluntary" are indeed often used as synonyms. Our conception of consciousness as a complex grouping and sequence of unconscious nervous processes implies a certain freedom of choice. As far as mere reflexes and habits are concerned, the distribution of forces runs in fairly well-established channels, determined by facilitation and inhibition, to gain the eventual final common pathway of action. The configurations of reasoned and

28. Bergson, H.: Essai sur les données immédiates de la conscience, Paris, F. Elcan, 1904; Matter and Memory, translated by N. M. Paul and W. S. Palmer, London, The Macmillan Company, 1911.

29. Jackson, J. H.: Selected Writings, edited by J. Taylor, London, Hodder & Stoughton, 1931, Vol. 1, pp. 186; Vol. 2, pp. 83, 143, 158, 159, 187, 189.

planned activity are of the same character, but more complex and unpredictable. When the introspective concept of the ego enters this configuration, we get the feeling of free will. Volition is not opposed to the laws of nature; it is their most complex implementation.[30] Choice is from a limited number of preceding alternatives only, which in any given instance depend on the individual range of knowledge and imagination. In fact, there is at any instant of choice or conflict a setting favoring one object at the expense of the one or many others, a tensional relationship between the figure and the background. The choice is the outcome of that tension, and action may restore a transient equilibrium. If rigid, the figure may have to yield as a whole and, fading away, become background, while part of all of what has been the former background is now taking the stage as figure. If this is true, the concept of contradiction may be resolved into a succession of figures, with alternations in the figure-background relation. In moments of stress or delay the ego-figure intervenes and lends to the performance the character of a dramatic personal decision.

Thus, "will" as it appears in popular usage, so far from explaining behavior, requires some such explanation as has been given. Bound up, however, with moral considerations, "will" is an old way of interpreting in retrospect the outcome of moral conflict. It is often said to have been "strong" or "weak" according to whether or not the resulting action is finding moral approval, in case the person has been aware of a dilemma. The question of consciousness and volition is also much entangled with the problem of legal responsibility, particularly when it has to be ascertained whether the defendant did "know that what he was doing was wrong." The interpretation in various contexts of such words and phrases as "to know," "to know what one is (or was) doing," and "to know what is wrong" is, to say the least, controversial, and beyond the scope of the present paper. To grant man a certain degree of free will is obviously justified and necessary on the grounds of common experience, and the appeal to this faculty usually can and must be left to common sense.

Statements to the effect that we are "after-conscious" in introspection and "behind the times" in perception imply that the factor of memory is never absent from mental events. Memory is, as it were, their afferent component, with its messages from the actual past. Similarly, volition, as an efferent agent, is in some form constantly at work and directed toward the future, which is "merely real without being actual" (Whitehead [24]). But the structure of consciousness is so compact that the afferent and efferent factors, the remembering and the preparing of action, continually embrace each other in that mysterious union called the specious present, and contribute to the grip we have both on the past and on the future.

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30. Obviously, this is a matter of belief or prejudice, not of proof. If a person sets out by declaring that "will" is a supernatural force, and defines it as such, no amount of research is going to dislodge him from this position. The upholders of absolute free will are irrefutable when they say that it cannot be reduced to natural processes, for the very reason that what they have agreed to call "will" is by that definition supernatural. Similarly, my attitude is motivated by the desire to make a hypothesis fit the existing evidence, rather than to submit to a dualistic dogma.

THE OBJECTIVE INQUIRY

William James[25] stirred the philosophical world by stating that consciousness was a function, and not an "entity," the function of knowing. How can we define the function of knowing in terms of nervous activity?

As we have seen in our discussion of the ego, it is a matter of terminological convention at what level of the phylogenetic scale we are to endow an animal with consciousness. There is equally no precise base line for conscious behavior at any moment in the life of any particular member of that species which we declare capable of it. Apart from electroencephalographic evidence, only efferent function can be objectively assessed, including, in man, the phenomenon of verbal behavior. This implies a great deal of unreliable data, and we get no definite answer to such questions as to whether, and what kind of, consciousness may be present in a state of epileptic automatism or in early stages of recovery from head injury. How does consciousness alter in its finer shades, encountered in introspection, problem solving, habit performance, daydreaming, distractedness, and actual psychotic distraction, in all those conditions in which the distinction between the degree and the kind of consciousness is blurred? (Distinctions do get blurred just when we look very closely in order to be precise.) Analyzing consciousness by experiment means disturbing, but not producing, it. The changes in electrical potentials evoked in the sensory cortex by stimulating the peripheral nerves indicate the unhindered arrival of sensory messages in the brain. But they are no less a feature of an anesthetized than of a conscious organism (Forbes and Morison[31]) and corroborate our thesis of the unconscious nature of isolated processes.

Degree and Kind of Consciousness.—Thus, in trying to define consciousness, we cannot establish either its lower or its upper limit. But two of its characteristics have been stressed by many: the qualitative and the quantitative. Hughlings Jackson[29] has already held that "there is no such entity as consciousness." On one hand, it varies by degrees; on the other, it varies as to its kind, i. e., according to the part of the higher coordinating centers involved. In other words, it is energy added to the energy already at work in the central nervous system, and is distributed over various channels. But Jackson also expressed the view that consciousness is "the most special of all nervous processes whatever," a view which will be discussed later. He distinguished between subject and object consciousness; this aspect has been dealt with in the previous section. His was the Cartesian dualism of mind and brain, the brain being merely the organ of mind. He wrote:

> It may be said that consciousness is a function of the brain. . . . This I deny. . . . We cannot take a too brutally materialistic view of the "organ of mind," but in order to do so we must not take a materialistic view of mind.

Consciousness as a mysterious epiphenomenon, arising parallel with organic activity, is still a very commonly accepted view (Martin[32]). Head's[33] concept of

31. Forbes, A., and Morison, B. R.: Cortical Responses to Sensory Stimulation Under Deep Barbiturate Narcosis, J. Neurophysiol. **2**:112-128, 1939.

32. Martin, J. P.: Consciousness and Its Disturbances, Lancet **1**:6, 48-53, 1949.

33. Head, H.: Aphasia and Kindred Disorders of Speech, New York, The Macmillan Company, 1926.

"vigilance" is one of quantity; consciousness is vigilance, or increased activity of Jackson's higher cortical centers.

That consciousness is a matter of degree,[34] and not an "all-or-none" affair, is a basic notion, again emphasized by Ingham [35]; it is a "state of activity of the entire central nervous system," activity which varies as to both its quantity and its kind; the quantity is dependent on the energy liberated by the hypothalamus. Cobb [36] also defined consciousness as "a function of nervous tissue in action, just as much as contraction is a function of muscle. . . . What is needed is a method that will quantitatively determine the amount of some physicochemical process that parallels what we already know about consciousness." In driving materialism and objectivism to their extremes, behaviorists have tried to do without the concept of consciousness. However remote and unreal the notion of consciousness becomes when we build up the integration of behavior on the conditioned reflex (Watson [37]), old practical concepts implicit even in the crudest observation of consciousness (as opposed to unconscious states) will reassert themselves. Babkin,[38] emphasizing the fact that a conditioned reflex can be formed without attention being focused on it, nevertheless conceded that "alertness" is necessary to start with.

The Time Factor.—Attempts at interpreting the working of the mind usually take into account the picture of a neuronal network immutably fixed in space; this picture is enlivened by the idea of rapidly traveling energy, shifting and shunting into kaleidoscopic spatial arrangements, like "one of the electric signs in which a pattern of letters passes rapidly across a stationary group of lamps" (Lashley [22]). We definitely have to take into account the time order in which these patterns gather, dissolve, and succeed each other. An "isolated instant" of consciousness would be a self-contradictory term.

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34. To establish the degree or depth of (un)consciousness is the common practice of anesthetists and all clinicians dealing with patients whose brain function is impaired. The mere division into "conscious" and "unconscious" is inadmissible, as it does not allow one to evaluate the progressive changes in the patient's condition. It is a commonplace, but not always realized, that these changes must be known in detail for efficient handling of the case. The details required are on more or less conventional lines and include a description of behavior and reflexes, supplemented, in patients recovering from head injuries, by retrospective accounts establishing the extent of retrograde and post-traumatic amnesia (Russell, W. R.: Cerebral Involvement in Head Injury: Study Based on Examination of 200 Cases, Brain **55**:549-603, 1932). Although we are unable to give the exact wave length, as it were, of any shade on the spectrum of consciousness, we can do better than limit our observation to its extremes, and should acknowledge the, admittedly ill-defined, states intervening between "deep coma" and "full consciousness."

35. Ingham, S. D.: Some Neurological Aspects of Psychiatry, J. A. M. A. **111**:665 (Aug. 20) 1938.

36. Cobb, S.: Borderland of Psychiatry, Cambridge, Mass., Harvard University Press, 1943, p. 100.

37. Watson, J. B.: Behaviorism: A Psychology Based on Reflexes, Arch. Neurol. & Psychiat. **15**:185-204, (Feb.) 1926.

38. Babkin, B. P.: Origin of Theory of Conditioned Reflexes: Sechenov; Hughlings Jackson; Pavlov, Arch. Neurol. & Psychiat. **60**:520 (Nov.) 1948.

"Time is required for consciousness," Jackson wrote. As Sherrington [39] put it:

There is no denying the extreme importance of the vast actual extent of the spatial conjunction of cerebral elements by conductive channels. . . . Yet I cannot but think that its limitless postulation leads not so much to explanation of the high degree of unity of the individual mind as to an ultimate fallacy which Prof. James has trenchantly termed that of "the pontifical cell." Pure conjunction in time without necessarily cerebral conjunction in space lies at the root of the solution of the problem of unity of mind.

How are we to understand this?

No constant stimulus of any length of duration is perceived as such. If it is long, we perceive bits of it, and mainly its beginning, then its end; at the end we remember the beginning and fuse the two events into one whole. In fact, I think, we simply establish one whole out of one or many couples of memories, the couples being composed of "on" and "off" effects. Our attention, no less than our thoughts, proceed in imperceptible little jumps. This discontinuity of stimulus effect, however, concerns contiguous or overlapping objects and thus gives us the impression of fusion. Adrian,[40] and Walter and Grey Walter [41] pointed out that changes in stimulus intensity, rather than steady or absolute, levels, are transmitted, rapid changes having a greater effect than slow ones. If we assume the structure of these events and of our way of perceiving them to be similar, the fusion which occurs in the percept is one in space, as well as in time. Whereas our laboratory methods are so devised as to perform an objective and indirect separation of smaller and smaller details, arranged in ever greater complexity, our mind works on wholes.

Balance and Rhythm.—Consciousness, one might cautiously say, is the state of successive nervous integration in which the greatest variety of cortical and subcortical connections is made possible. A field of forces is holding itself in a manner so precariously balanced that a maximum of potentialities is insured, potentialities for slight disintegration into part action. This disintegration normally alternates with reintegration in a form of pulsation. It is this rhythmical balance which in consciousness guarantees the to-and-fro control over activities scattered in space and in time. Each inner impulse demanding attention tends to upset the ideal equilibrium (Herrick [42]). Then the circuits or subfields responsible for one particular activity become more definitely isolated from the rest, and the ideal state of consciousness deteriorates. Cobb [43] put it this way:

In such a state attention is usually directed to certain objects with neglect of others. Therefore there is never a state that could be called full consciousness.

It seems reasonable to assume, however, that in these fairly rapidly changing pulse patterns the process of breaking up of largest circuits and the narrowing down

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39. Sherrington, C. S.: The Integrative Action of the Nervous System, London, Cambridge University Press, 1947, pp. 38, 45-67, 207-214.

40. Adrian, E. D.: General Principles of Nervous Activity (Hughlings Jackson Lecture), Brain **70**:1-17, 1947.

41. Walter, V. J., and Grey Walter, W.: Central Effects of Sensory Stimulation, Electroencephalog. & Clin. Neurophysiol. **1**:57-85, 1949; The Electrical Activity of the Brain, Ann. Rev. Physiol. **11**:199-230, 1949.

42. Herrick, C. J.: An Introduction to Neurology, Ed. 5, Philadelphia, W. B. Saunders Company, 1931, p. 356.

43. Cobb, S.: Foundations of Neuropsychiatry, Baltimore, Williams & Wilkins Company, 1941, pp. 83, 85.

into smaller and more isolated ones is periodically reversed. Each such reversal or return to the base line is a brief "diastole," or "refractory period" which restores fuller consciousness. The old principle of rhythmicity as a property of physical processes, and of nerve tissue in particular, may find an application to the understanding of consciousness. Rhythmicity in the central nervous system is found on a "macroscopic" scale in the effect of the respiratory centers on the respiratory muscles, in Sherrington's "successive induction" applicable to the walking mechanism, and in the clonic character of the scratch, swallowing, blinking, and stepping reflexes, all due to the refractory state. This state, or hypothetical metabolic requirements of the nerve cell for alternating anabolic and catabolic processes, may explain some of the puzzles of variable excitatory and inhibitory effects following stimulation of identical points in the nervous system, as reported by Dusser de Barenne and McCulloch,[44] Liddell,[45] and Babkin and Kite.[46] The application to physiology of reverberating circuits, scanning, and the feed-back principle, emphasized by Wiener [47] and others, may be another instance of alternating release and restraint.[48] On a "microscopic," or electronic, scale, this rhythmicity finds its obvious expression in the biphasic action potential of neuronal activity, i. e., the constant effect polarity has on the wave pattern to make it swing back to the isoelectric position of equilibrium. It remains to be seen whether such generalizing speculations are acceptable; similar claims have been made, for instance, by Goldstein.[7]

Isolation; Disintegration; Preservation; Confusion.—Such rhythmical respite as has been postulated for the maintenance of consciousness in attention may, however, be prevented by fatigue or disease. A relatively small pattern of brain activity may be left beating in isolation (Kubie [49]; Goldstein [7]), and the large whole becomes incapable of re-forming completely. In that case there may result preservation or some other form of motor, sensory, or ideational automatism, such as rebound, after-image, tremor, hyperkinetic phenomena, reiteration of a part of an attempted task, amnesia, and possibly hallucination and delusion. On this hypothesis, further failure to remedy the break-up results in confusion, i. e., when large intervening cerebral territories are silenced by seclusion and a number of fields act in isolation. It may seem paradoxical that in mildly disturbed consciousness perseveration occurs together, or alternates, with distractibility. Their common

44. Dusser de Barenne, J. G., and McCulloch, W. S.: Factors for Facilitation and Extinction in the Central Nervous System, J. Neurophysiol. **2**:319-355, 1939; Functional Interdependence of Sensory Cortex and Thalamus, ibid. **4**:304-310, 1941.

45. Liddell, E. G. T.: Integration, Then and Now, J. Neurol. Neurosurg. & Psychiat. **12**:81-85, 1949.

46. Babkin, B. P., and Kite, W.: Central Nervous Control of Gastric Motor Function, to be published.

47. Wiener, N.: Cybernetics or Control and Communication in the Animal and the Machine, New York, John Wiley & Sons, Inc., 1948.

48. A particularly felicitous recent concept is Hebb's "phase sequence," stressing the importance of timing in the "assembly" of neural pathways and the reinforcing or disruptive influence of sensory and motor events on the current central organization (Hebb, D. O.: Organization of Behavior: Neuropsychological Theory, New York, John Wiley & Sons, Inc., 1949).

49. Kubie, L. S.: Theoretical Application to Some Neurological Problems of the Properties of Excitation Waves Which Move in Closed Circuits, Brain **53**:166-177, 1930.

feature, however, is the failure of part activity to become integrated into more articulate complexes. The patient is either unable to pay more than a very poor sort of attention to his performance, which consequently becomes progressively stereotyped and, with reference to the task in hand, incoherent. Or he cannot fix his attention at all and falls a victim to stimuli which have no bearing on his task. In our concept of consciousness, the abilities of focusing and defocusing are equally important; perseveration and confusion are the result of an interference with their smooth succession. Good articulation, *Prägnanz,* i. e., the precision of what is handled in consciousness, is not due to a rigid quality of the mental patterns, but owes its efficiency to their malleability and the ease with which they allow themselves to be taken apart and again incorporated into other processes. Thus, "concentration," though the first step into the blind alley of perseveration, is distinguished from the latter, and the distinction is seen in the ability of a conscious person to stave off further disintegration by leaving off the task. In so doing, he turns to something else through "fuller" consciousness. Detachment is thus at least as important an ability as concentration; these two alternate when we are conscious.

Epilepsy.—Jackson, and, after him, mainly Penfield, have taught us much about consciousness by studying its derangements in the epileptic attack. In the various forms of epilepsy the whole field of consciousness is violently broken up. An excessive current, springing up or induced in a subsystem of neurons, active in heightened synchrony, either is spent locally to produce a focal seizure or spreads and swamps a large field in a generalized attack. In the case of a focal cortical seizure the affected part of the body is lost to voluntary control or is subject to a sensation not provided by a true environmental stimulus. In other words, the affected part is to all intents and purposes paralyzed, as far as the patient is concerned, though manifestly it is the victim of convulsions or hallucinations (Penfield [50]). Of such partial disturbance or function the patient is aware, but only as of some extraneous, strange, and rather frightening event. Of this he has a kind of second-hand experience, which differs from his healthy feelings of movement, touch, sight, etc., for these are normally related to his ego concept.

Psychomotor Seizures and Recognition: Further removed from reality and consciousness are the patient's experiences in psychomotor, or, as Penfield has termed them, psychoparetic seizures. These have a dream-like character, including vague recognition ("déjà vu"), fusion, or distortion of environmental stimuli and intrinsic feelings. Psychoparetic seizures seem to take their origin in pathologically altered, developmentally old parts of the cerebral cortex (archipallium) (Jasper [51]) as do also those hallucinatory auras which involve sensations referred to the viscera and the primitive, chemically stimulated senses of taste and smell. The most characteristic common feature of psychoparetic seizures is the disturbance in recognition, according to McDougall,[52] "that fundamental, rudimentary . . . judgement of sameness—Hello! Thingumbob, again." The archipallium is the part of the cerebral mantle developed from the amphibians onward. It seems likely that it can

50. Penfield, W.: Epileptic Manifestations of Cortical and Supracortical Discharge, Electroencephalog. & Clin. Neurophysiol. **1**:3-9, 1949.

51. Jasper, H. H.: Personal communication to the author.

52. McDougall, W.: Outlines of Psychology, New York, Charles Scribner's Sons, 1923, p. 308.

organize patterns of a crude kind only, a mixture of affective recognition, affirmation (or rejection), and belief. This may be the basis of personality and of primitive value judgments, while the weaving of the subtler and more unstable patterns of distinctive thought needs the participation of neopallial areas. There may, indeed, exist an older system of connections between the hypothalamus and the archipallium, dealing with this primitive and fundamental way of accepting and rejecting somatic impulses and visceral messages carrying an emotive charge (Papez [53]; Cobb [54]). This system may be distinguished from thalamoneopallial circuits. These fail to take in large parts of the temporal cortex and of the inferior and medial surfaces of the frontal lobe and are used in more precise discrimination. Klüver and Bucy [55] described a form of "psychic blindness" following bilateral removal of the temporal lobes in monkeys; the confused and aimless behavior of these animals may be interpreted in the light of this common factor, i. e., the want of crude recognition.

While dream-like experiences are conceivably initiated by the predominance of archipallial, i. e., crudely recognitive activity, the characteristic feature of true dreams is seen in the dissociation of neocortical or whole-brain mechanisms. Hence, their uncritical and hallucinatory antics, their tendency to fuse and confuse, in space and time, what to common sense is vaguely or not at all related. Although there is no "lesion," the absence of sensory stimuli and other check mechanisms makes for the break-up of over-all cerebral organization. (In mentioning but briefly the disconnected, and, as it were, clotted, processes of dreams, I do not wish to exclude their dynamic possibilities, as postulated by psychoanalysts.) As a definition, one might suggest that dreams are those mental processes occurring in light sleep which are only just well enough organized to allow a more or less dim form of recall, subsequent recall being one of the criteria of consciousness.

Petit Mal: A mere loss of consciousness occurs in the petit mal type of seizure; with it all manifestations of cortical activity disappear both for the observer and for the patient. It has been shown electrographically by Morison and Dempsey,[56] by Jasper and Droogleever-Fortuyn,[57] and by Penfield and Jasper [58] that the generalized, bilaterally synchronous, 3-per-second spike-and-wave rhythm, characteristic of petit mal, can be reproduced in animals by rhythmical stimulation of the midline intralaminar nuclei of the thalamus. Whether such discharge is necessarily followed by complete loss, or impairment only, of consciousness, and whether these thalamic nuclei are to be considered as the "origin" or the "pacemaker" of the discharge picked up in the cortex, it may be taken for granted that consciousness depends on circuits which include the brain stem. Both this upper part and lower parts, includ-

53. Papez, J. W.: Proposed Mechanism of Emotion, Arch. Neurol. & Psychiat. **38**:725-743 (Oct.) 1937.

54. Cobb, S.: Emotions and Clinical Medicine, New York, W. W. Norton & Company, Inc., 1950.

55. Klüver, H., and Bucy, P. C.: Preliminary Analysis of Function of the Temporal Lobes in Monkeys, Arch. Neurol. & Psychiat. **42**:979-1000 (Dec.) 1939.

56. Morison, R. S., and Dempsey, E. W.: A Study of Thalamo-Cortical Relations, Am. J. Physiol. **135**:280-292, 1942.

57. Jasper, H. H., and Droogleever-Fortuyn, J.: Experimental Studies on the Functional Anatomy of Petit Mal Epilepsy, A. Res. Nerv. & Ment. Dis., Proc. **26**:272-298, 1947.

58. Penfield, W., and Jasper, H. H.: Highest Level Seizures, A. Res. Nerv. & Ment. Dis., Proc. **26**:252-271, 1947.

ing the reticular substance of the medulla (Magoun [59]), profoundly modify the electrical activity of the whole cortex. The activity of the intralaminar nuclei is different from that of the thalamic nuclei, which have a pinpoint representation on the projection areas of the cortex. The connections responsible for the petit mal rhythm are more diffuse, have a slower conduction rate, respond to lower frequency rhythms, and are fired under light anesthesia. One might speculate that these multisynaptic, slow connections are related to the delayed character of processes giving rise to consciousness and to the "diastolic" effect referred to above.

Brain Stem, Cortex, and the "Seat of Consciousness."—The fact that interference with various rhombencephalic and diencephalic structures produces, more or less differentially, either sleep or deeper levels of unconsciousness has been maintained since 1890, by Mauthner,[60] and later by Troemner,[60] Breslauer,[60] Reichardt,[60] von Economo,[61] Kleist,[62] Ranson,[63] Penfield,[64] Ingham,[35] LeBeau,[65] Jefferson,[66] and many others. These various contiguous parts of the brain stem have therefore been said to harbor the "seat of consciousness." Hardly anyone disputes the essential part the brain stem plays in combining, connecting, and conveying the part processes responsible for the unity of mind, for the brain stem emits and receives streams of potentials along its neuronal connections to and from the cerebral cortex. On the other hand, it has been maintained, e. g., by Martin,[32] that the role of the cortex in matters of gnosis, praxis, speech, and thought cannot possibly be underrated, for these functions are the essential characteristics of consciousness in those organisms in which the corresponding cortical areas are developed. "However," Penfield [58] wrote, "it is apparently not in the cortex that these complex functions are integrated into a coherent stream of conscious thought and action." "Integration" can mean only complete formation of a whole, and one will witness disintegration wherever a field, chain, or circuit is broken. The brain stem in isolation is incapable of maintaining higher degrees of alertness in mammals; it does so only when connected with cortical areas, which give its activity meaning and expression. It is, in fact, as little capable of assuring consciousness as is the isolated cortex when deprived of its main routes of rapid connection running through the thalamus (Walker [67]). Thus, Adrian [68] stated, "The whole mechanism certainly involves both the cortex and the optic thalamus as well as the brain stem." Even if the diencephalon, or the rhombencephalon, for that matter, is assumed to have on the cortex a dynamogenic or energizing influence, this is only of a modifying nature,

59. Magoun, H. W.: Caudal and Cephalic Influences of the Brain Stem Reticular Formation, Physiol. Rev. **30**:459-474, 1950.

60. Cited by Kleist, K.: Gehirnpathologie, Leipzig, Johann Ambrosius Barth, 1934, p. 1295.

61. von Economo, C.: Sleep as a Problem of Localization, J. Nerv. & Ment. Dis. **71**:249-259, 1930.

62. Kleist, K.: Gehirnpathologie, Leipzig, Johann Ambrosius Barth, 1934, p. 1295.

63. Ranson, S. W.: Somnolence Caused by Hypothalamic Lesions in the Monkey, Arch. Neurol. & Psychiat. **41**:1-23 (Jan.) 1939.

64. Penfield, W.: The Cerebral Cortex in Man: Cerebral Cortex and Consciousness (Harvey Lecture), Arch. Neurol. & Psychiat. **40**:417-442 (Sept.) 1938.

65. LeBeau, J.: Localization cérébrale de la conscience, Rev. canad. biol. **1**:134-156, 1942.

66. Jefferson, G.: The Nature of Concussion, Brit. M. J. **1**:1-5, 1944.

67. Walker, A. E.: The Primate Thalamus, Chicago, Chicago University Press, 1941.

68. Adrian, E. D.: The Physical Background of Perception, London, Oxford University Press, 1947, pp. 77, 85, 86.

for the activity of the isolated cortex, as demonstrated by Bremer[69] and by Kristiansen and Courtois,[70] is autochthonous, or spontaneous. However powerful an instrument this cell station in the brain stem may be, the term of a "center" or "seat" of consciousness does not seem apposite. One would hesitate to call the heart the seat of circulation, although it is its main motor and, together with the main distributing blood vessels, occupies a central position. Even a muscle cannot be said to be the seat of contractility. "Consciousness," "circulation," "contractility," are convenient abstract terms signifying the organization of complex processes in complex anatomical structures.

This question is one of logic and common sense as much as it is of anatomy and physiology. Everyone accepts the fact that spatially extended objects may be represented in two ways: by copies and by symbols.[71] Thus, three-dimensional parts of the body are represented by, in fact connected with, somewhat similarly shaped cerebral areas. A cortical projection zone, whether we see it as two- or three-dimensional, is something between a copy and a symbol of the part it represents. It is, at any rate, extended and palpably material.

Accepting, however, the representation in the brain of, say, the thumb or the retina raises more questions than it answers. Is it individual muscles or patterns of movement that are mirrored? What is the sensory or kinesthetic representation of movement? Are there small-scale models of what we see set up in the visual cortex? Of these questions there are many. It may even be argued that we are already transgressing descriptive rigorousness when we speak of "vision" being "localized" in the occipital cortex. Vision, as opposed to the extended structure of the retina, is a wide generalization and depends on a wider field than that of Area 17, wider, if its full implication is considered, than the occipital lobe. Or a smile, or the winding up of a watch, or any fleeting and never precisely recurring event—can it have focal representation? Has time, the fourth dimension, any topographical correlate in the central nervous system? Lashley[72] pointed out the discrepancy between the current terminology of behavior and the spatial arrangements of cortical areas, the difficulty of accounting for the ordered succession of movements, etc. With regard to the association areas, there are, among others, Koffka's[73] speculations on spatially extended memory traces and the processes which, as it were, ferret them out. Equally difficult to conceive are the more recent hypotheses of "scanning" (Walter and Grey Walter[41] and others).

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69. Bremer, F.: Quelques propriétés de l'activité électrique du cortex cérébral "isolé," Compt. rend. Soc. de biol. **118**:1241-1244, 1935; Considerations sur l'origine et la nature des "ondes" cérébrales, Electroencephalog. & Clin. Neurophysiol. **1**:177-193, 1949.

70. Kristiansen, K., and Courtois, G.: Rhythmic Electrical Activity from Isolated Cerebral Cortex, Electroencephalog. & Clin. Neurophysiol. **1**:265-272, 1949.

71. Copies and symbols are the respective extremes on a scale of structural similarity. Nothing can be a complete imitation of another thing; no matter how striking the resemblance, a copy must to some extent have the abstract character of a symbol. On the other hand, some symbols are merely very schematized copies; others, such as words, hardly resemble the things for which they stand, and numbers are but symbols of symbols.

72. Lashley, K. S.: Functional Determinants of Cerebral Localization, Arch. Neurol. & Psychiat. **38**:371-387 (Aug.) 1937.

73. Koffka, K.: Principles of Gestalt Psychology, New York, Harcourt, Brace & Company, Inc., 1935, pp. 65, 319, 330.

But in all these questions we are dealing with part action, and it may not be necessary to abandon mechanistic concepts, which have proved their value in physiological theory and medical practice. In consciousness, however, we are dealing with an altogether different plane of both verbal abstraction and synaptic diversity. It is indeed a term for summing up over-all activity, an abbreviation of the most efficient integrating and differentiating activities of every sort and variety. By definition, consciousness is not just another function belonging to the same category as hearing and seeing. It enters into each of these, as well as including them all. Jackson's words of it's being "the most special function of all" can, it seems, be interpreted only in the sense that it has such wide and general application, potentially pertaining to any and every kind of nervous activity which is not isolated.

It might be objected that an injury to the brain stem causes unconsciousness, or even death. In death there are no units, in unconsciousness a relatively small number, and in consciousness a large and growing number, actually and potentially cooperating. A lesion of the lower brain stem produces not only unconsciousness, but respiratory and vasomotor paralysis, and the animal dies. Is the injured agglomeration of cells the center of life? An alteration in the state of the upper brain stem renders the organism unconscious by modifying impulses necessary for consciousness. Are we justified in taking "loss of consciousness" in its literal sense, implying that a concrete entity has been driven from the seat where it had dwelt? Not unless we unduly strain a metaphor and give, in the words of the "Midsummer Night's Dream," "to airy nothing a local habitation and a name." "Although medical men speak clinically of loss of consciousness as if there were a well defined entity called consciousness" Jackson wrote, "there is probably not amongst educated persons any such belief."

"Full Consciousness."—Thus, the brain stem may be called a channel, a gateway, a modifier, of currents which in their figured entirety constitute consciousness. What parts of the brain, in addition to the brain stem, are involved in "full" consciousness? When is the unity of the mind achieved? Adrian,[68] discussing the disappearance of the alpha rhythm during attention, drew the conclusion that "full consciousness is possible where the direction of our attention has made the cells accessible to the messages which reach them." This is determined "by a balancing of claims which must take place in some central region to decide which part of the cortex shall be set free from the alpha rhythm for the use of the mind. There should be differential rather than uniform activity in some part of the cortical area, though not necessarily in a very large part." Such words are reminiscent of Jackson's phrase, "that we are from moment to moment differently conscious." In a negative sense, Martin's [32] "sectional" disturbances of consciousness due to selective cortical lesions belong to the same line of thought.

"Full" consciousness, however, is probably a misnomer, unless we make it equivalent to our hypothetical concept of that "diastolic" instant just before or after attention is being or has been focused, of that brief interval when a great many potentialities of engaging this or that part of the cortex are open. It is questionable whether such a state of passive preparedness can be prolonged; it then would correspond to the condition of the "empty mind," i. e., that attitude of shutting out, with closed eyes, all external stimuli, "trying not to think of anything." This condition, of course, produces the alpha rhythm, and one wonders whether that back-

ground synchrony is the expression of the "fullest" consciousness of which we are, after all, capable. A yogi might consider just such a state as the highest and ideal form of being conscious. In Todman's [27] behavioristic language, the relatively disinterested and nonpractical character of "consciousness-ability" is stressed, the "behavior-adjustment to, or mere behavior-feint at, the running-back-and-forth" attitude of puzzled rats. In a similar vein, Dewey [74] saw reflection appear "when there is some trouble due to conflict, when a situation becomes tensional," and Whitehead defined consciousness as the "subjective feeling" of the contrast between what is "in fact" and what "might be."

To me, it seems best to regard ideal or full consciousness as being of a potential nature, expressing the freedom of any part of the brain to communicate with any other, as well as to preserve and to prepare the past for the future. Consciousness, like knowledge, is a meaningless term if it is conceived in isolation and as the function of a central agency alone; it gains meaning only if it includes its objects, i. e., the totality of patterned messages traveling along peripheral and central nervous pathways, corresponding to memories and relevant features of the environment.

Thus, the current division into the topographical, or qualitative, and the energetic, or quantitative, aspect of consciousness, as stated at the beginning of this section, becomes somewhat inadequate. As in nuclear physics, the distinction between the particle moved and the force moving it has been abandoned for a concept of form, so in our field structure and function must appear even more inseparably united than hitherto. Summation is not one either of energy or of the neurons carrying it, but of both as a whole. The degree of consciousness depends as much on the organization of topographical relationships as does its kind or content. Indeed, degree and kind are indistinguishable. We are not, on the one hand, more or less conscious, and, on the other, conscious of different objects; rather, the degree makes a difference to the kind, and the kind to the degree. Whether an object appears bright or dim, precise or vague, depends both on the amount of energy it summons into action and on the kind of organization it evokes. Intensity and form of experience are no independent variables.

ORGANIZATION OF CONSCIOUSNESS

In the foregoing discussion, the attempt has been made to bring together, and at the same time to keep distinct, the physical structure and processes of the central nervous system, on the one hand, and the concepts of mental analysis and synthesis, on the other. In concluding, some doubt remains whether it is favorable to knowledge "to cross frontiers," the frontiers being made formidable by excessive differences between sets of magnitudes, between sets of reference, and between the principles of chance and of plan. Do we gain anything by assuming that some power called form or organization or Gestalt—apart from, or synonymous with, the all-pervading concept of energy—enables parts to become a whole? One and the same object yields different aspects when we look at it closely and when we stand back; each of these attitudes is conducive to knowledge. But can we grade and integrate the results of our attitudes without ensuing contradictions?

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74. Dewey, J.: Essays in Experimental Logic, Chicago, Chicago University Press, 1916, p. 11.

"Homologous" Parts of Nervous System; Importance and Value of Various Areas.—Let us glance once more at the organization of consciousness. The conscious human being, the most complex organized unit known to us (excluding society), can be analyzed into less complex parts. Such parts have features resembling the parts of less complex forms of life, sometimes resembling such whole forms themselves, e. g., phagocyte and ameba. Resemblance of form and function, however, is not identity. Man, obviously, is not an assemblage of unicellular organism, nor is he a heap of organs. There is organization, mutual interaction. But in members of different species even homologous parts differ in relation to the whole organization of any member. Thus, the spinal cord is for the frog a relatively more complex or advanced structure than it is for the dog; the decapitated "spinal" frog is a more satisfactorily integrated residual whole than the spinal dog. "Progressive encephalization" has two aspects; one is the shift of function to the "new" structure of the "higher" organism; the other, the lowered status of those older structures which have been surpassed by the newly acquired ones. There is both addition and the establishment of a new equilibrium between parts. Without suffering gross paralysis, the dog can dispense with the motor cortex, as though it were a luxury; man is less fortunate, since for his limbs the motor cortex is much more essential. Man's most highly valued structures are his "recent" association areas; yet he can afford to part with a good deal of them and still get on in life somehow. Paradoxically, we thus value most highly that which is most superfluous; and we estimate as lower in value the mere necessities. A newborn baby, for instance—is he the most precious and, at the same time, the least essential member of the family, speaking in terms of the actual present rather than of the potential future? Importance and value are not synonyms.

The primitive nervous system of lower animals has to serve both vital and specific functions, in conation and cognition; where differentiation is poor, the "cheaper model" has essentially to perform that which a more expensive one does, only not performing it all quite so elaborately and precisely. But the cheap model has its own safety margin as regards loss and injury; it preserves function in its own way despite wear and tear. Although it will not play such a welter of adaptive tricks, the few it can play are played amazingly well. An earthworm, cut in two, may be said to develop two separate egos; at any rate, each of these is no worse off (and perhaps no better) than a man after frontal lobotomy. It is as though the worm's ganglionic chain were "homologous" not only, as one would think on anatomical grounds, to man's autonomic nervous system, but also to the spinal cord, brain stem, and projection and association areas, as far as function is concerned. Although less differentiated, and having its functions more concentrated in space, it has them at the same time more diffusely spread. We have to divide the worm into many bits before hitting its "vital center," planned very differently from ours.

Differentiation; Encephalization.—One of the many difficulties in understanding evolution is its four-dimensional character, i. e., the dynamic character of "structure-in-function." According to Coghill,[75] individuation brings about a new relationship between a part and the whole of the developing organism or species. Proliferation and differentiation from a relatively equipotential, growing system are thought to

75. Coghill, G. E.: The Neuro-Embryologic Study of Behaviour: Principles, Perspective and Aim, Science **78**:131-138, 1933.

result in that expansion and individuation which we find in "learning." This view I wish not to oppose, but to amplify by the suggestion that the latest developmental acquisition is, in itself, the least differentiated and specialized. We may, again, distinguish roughly between rigidly fixed patterns of integration, which we may call old, and the remaining or increasing part of the matrix from which they were once developed. This matrix is still multipotential and capable of change and growth; it also has the capacity for forming new, and as yet unstable, patterns. In this sense, Coghill's individuation or differentiation, representing that which, in the widest sense, has been "learned," is only the last-but-one step in development. There is, we think, a later stage, exemplified by those structures from which change and increase may be expected phylogenetically (association areas); this finds its functional expression ontogenetically in progressive learning, as opposed to fixed mechanisms, either innate or acquired earlier in life.

The "older" a mechanism, the less versatile and dispensable is its function. Man's specialized motor projection area is "older," and more important for his motor apparatus, than the same area is for the animal's limbs. On the other hand, a hemiplegic animal is biologically so handicapped that we may humanely put it to sleep, whereas blind, deaf, or paralyzed men can be creative members of their society, and self-satisfied. While such men cannot regenerate the lost function, they can compensate for it from the rich store of roundabout, interchangeable, symbolic faculties. This power of adaptation is derived from a safety margin lying in the bulkier, unspecific, more intelligent human association areas. "The silent" cortex of man vouches for a fuller consciousness—one more voluminous, precise, and imaginative. Not only is man more receptive, and to a greater variety of stimuli, but his ability to analyze and synthesize them is also more elaborate and exact. Degrees of consciousness in man and animal are therefore comparable only up to a point. Grossly speaking, the anesthetist's data, or those of an observer who would be able to measure fatigue, do apply to a man, as well as to an animal. But not only is man capable of being more fully conscious; at each stage, exceeding the animal's optimum, his consciousness is differently and more subtly organized.

Levels.—If such considerations are valid, if differentiation is a matter of organization and quality, rather than one of quantity and degree, the validity of a hierarchy of levels may need to be reconsidered. We may believe that the concept of evolution is correct, that the complex is a product of growth and summation of the simple, and that consciousness has its source in unconscious processes. But when we come to examine unified complexity, we wonder whether it is expressible in terms of focal re-re-representation. In any given central nervous system, specialization, so far from increasing, does, in fact, diminish as we ascend from the periphery to the brain stem, and from the projection areas to those of association and elaboration. It must be assumed that the greater part of the human cortex is relatively equipotential in function (Lashley [22]), or at least multipotential as compared with the projection systems. There is a branching and tree-like spreading out, a giving up of the principle of centralization, as we ascend from the brain stem to the cortex. Of all levels, the existence of the highest has always been the most difficult to conceive and to accept. As a relative and ambiguous notion, it renders precarious the whole theory of levels. Can this be saved by the attempt of placing the highest level in the upper brain stem, according to Penfield and Jasper [58]?

It is true that bare consciousness depends on an intact brain stem with little cortex attached to it, while all more complex and successive mental activity requires a proportionately greater amount of functioning cortex, both silent and eloquent. So long as we consider man as the highest animal, because he is physiologically the most complex, biosocially the best adapted and most powerful, and ethically the most moral (though this is denied in some Eastern religions and often doubted even in the West), so long as we consider the human species as the top of a natural hierarchy, we, by the same token, attribute to the brain the highest status in man's organization. On these grounds, it would still be the cortical association areas which give the human brain its special dignity. But knowing that this highest value—as it were, man's cortical library, art gallery, theater, concert hall, laboratory, and study—is worthless without mechanisms on other levels, acting as power station, mine, field, and factory, transport system, and sewer, we may begin to doubt whether this metaphor of a hierarchy is not altogether a cul-de-sac for biological thought. Even if we grant the brain stem the position of a selecting and distributing agency, and place in it the origin of an extramotor and extrasensory system, we have to admit that it can select and distribute only such material as it gets from the peripheral analyzers and from various parts of the cortex, and that it is subject to the tensions existing in fields bearing upon it. There are didactic reasons for keeping up the simile of a House of Parliament in the terminology of segmental and cerebral "representation"; there are good grounds for describing phylogenetically older and newer mechanisms of integration, and there is safe evidence of the to-and-fro projections between the basal and the cortical gray matter. But it does not seem necessary or justifiable to place at some highest level an executive and jurisdictive ruler as the last instance of control over consciousness. Levels may well be nothing but gross artifacts produced by simplifying the analysis of toxic, traumatic, and other lesions inflicted by experiment or disease (Goldstein [7]). The more complex a manifestation, or the more complex it becomes as we study it, the greater our caution must grow in drawing inferences from the particular to the general.

A great deal of fundamental terminology is equivocal. With regard to cerebral function, the word "complex," for instance, designates both the developmental deposits of specialization and the versatility of undifferentiated units. More confusing still, and less helpful, become terms like "higher" and "lower," if we are asked, as it were, to climb up and down the anatomical, altitudinal structures. The key position in which we find or put the brain stem is another dangerous metaphor.

Broadly speaking, Jackson's pioneering concept is still ours, namely, that the highest, or most complex, processes of the association areas are the least rigidly organized and the most heterogeneous. But the hypothesis of three distinct "levels" was conceived at a time when it may have appeared possible to identify such levels with synaptic relays. Since then, the system of neuronal connections has revealed its most complex, extensively multisynaptic nature. It has also become impossible to see in the cortex a terminus for incoming and outgoing messages. The cortex cannot be viewed independently of subcortical influences and vice versa. The facts of this mutual interaction, in particular, the discovery of electrical "driving" from structures as low as the reticular substance, have been

well established (Magoun[59]). In addition, we know that the effects on consciousness produced by damage or isolation of the frontal association areas are relatively small, and we may assume that the neurons of the "silent" areas are equipotential or multipotential. All this points to the necessity of reconsidering and modifying the concept of levels.

We are faced with the problem of reconciling the theory of mechanical, isolated, and universally homogeneous reflex action with observations of heterogeneous, mutually tensional field and Gestalt organization. "As life develops," Sherrington said, "'conscious' behavior tends to replace reflex." "These transitions," to quote Adrian[40] "are hard to understand, but it is still harder to believe that we are confronted by some radically different kind of nervous control."

When in conceptual difficulties, we hope to get assistance from a simile. While aware of the necessary reservations, we cannot help likening the plan of the biological entity which is the conscious being to such mechanical structures as surround us in our man-made everyday life. Let us take a much less complex phenomenon as a model for our organic one, say, a passenger train. There are coaches with their fittings, connected among each other and to an engine, with its fuel; there are an engine driver and other personnel, with all their past and future, their families, salaries, insurance policies, and hobbies; passengers and luggage; rails, points of start and destination, and a railway company, with its workshops and offices, its shareholders (as the case may be), and its maps and timetables. Indeed, our list can never be complete, and the less so, the more we study all that the train implies, for we are gradually drawing in the universe. We shall never be able to tell exhaustively, either in one sentence or in many books, how and why the train runs or is being run. Nor shall we be able to put our finger on what is the most essential of its parts or establish a hierarchy between those parts. We may best approximate the truth by taking the whole organization, with all that it implies when the train is running, and say that this is about the highest level it can reach, higher, at any rate, than is any of those parts on our list. And our train, we remember, is a much less highly integrated unit than our conscious man. Yet even in taking this holistic attitude, we shall not escape the just criticism of holding vague and tautological notions.

SUMMARY

Summaries, definitions, or abstracts, by omitting detail and presenting only salient, spotlighted features, are much in the nature of aphoristic caricatures. We gain by beholding a pattern of highlights, but we lose by the distortion of condensation.

Consciousness produces such summaries; the selections it makes consist of rapidly alternating analysis and synthesis.

The hypothesis is presented that consciousness is rhythmic and cyclic; a rapid succession of slight disintegration during attention, alternating with intervening returns to a base line of restitution, guarantees the characteristic greatest potential variety of ever-changing connected patterns, or "phase sequences" (Hebb[76]). Detachment is as important a feature as is concentration. This alternation may

76. Hebb, D. O.: Organization of Behavior: Neuropsychological Theory, New York, John Wiley & Son, Inc., 1949, p. 145.

be achieved by the phasic character of neuronal discharge, based on catabolic and anabolic processes, and grouped and regrouped by fields of energy. Deterioration of consciousness, more permanent and irreversible than sustained attention, begins with perseveration and increased distractibility; this is given by fixation and isolation of processes.

Exclusively physiological and exclusively introspective accounts of our subject are incomprehensive and give rise to artifacts. Although they are complementary, integration of knowledge is hard to achieve because their points of reference and scales of observation are wide apart.

Like "life," consciousness is a logical construction. In this presentation, it is the organism which is held to be conscious; thoughts, images, the ego, etc., are contents or parts of the conscious organism. The ego is a convenient abbreviation, an abstract in both senses of the word, of an antecedent object, or a multiplicity of objects, from which it is developed.

Consciousness arises when unconscious processes are integrated; its base line in the individual and in the animal kingdom is arbitrary.

Consciousness can have no "seat," any more than terms like circulation or contractility. It is not either cortical or thalamic. The diencephalon and rhombencephalon have to be intact for an animal or a man to be alert, wakeful, or conscious and for the cortex to function adequately. Consciousness has no meaning without its contents, which are supplied by the periphery, as well as by the cortex.

Integration of consciousness is not contrived by any one part; it is the expression of a plan acted on by a whole.

The establishment of levels, both of consciousness and of function represented in the central nervous system, though didactically useful, is probably too artificial. Usually "high" and "low" merely imply a quantitative scale of value and degree; in fact, we are dealing also with the qualitative aspects of organization.

Specialization of function is a deposit of evolution and habit formation; the most recent "silent" areas of the cortex are relatively multipotential.

Had I been able to procure E. G. Boring's "Physical Dimensions of Consciousness" (New York, D-Appleton-Century Company, 1933) before or during the writing, it is uncertain whether the comprehensiveness and lucidity of this book, its affinity, and apparent parentage would have acted as an encouragement or a deterrent to putting on paper what I thought were my own ideas. Under the circumstances, I regret not having been able to refer to it in many places.

BLOOD EOSINOPHILIC LEUCOCYTES IN MENTAL DISEASE

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PSYCHIATRISTS of half a century ago were aware that changes in the blood eosinophilic cell count occurred in mental disease [1]; it was recognized at that time that remission was often accompanied by eosinophilia and that a persistent abnormally low count indicated a poor prognosis. Since then a large and discordant literature bearing on the problem has developed; this has been reviewed by Rud.[2] Confusion concerning the relation between mental diseases and changes in the blood eosinophil count arose because almost all the older workers used methods of low accuracy and because, in addition, there was a high incidence of infection with protozoan and metazoan parasites in patients in hospitals for mental diseases.[3]

The reintroduction of methods for the direct enumeration of blood eosinophilic leucocytes has made it possible to measure accurately changes in the blood eosinophil count; accordingly, the present study has been made.

MATERIAL AND METHODS

Blood eosinophil counts were made as described previously [4]; 25 were made on normal subjects and 244 on untreated patients. The effect of a course of ambulatory insulin or electroshock treatment was studied in 118 patients, and the influence of pregnancy was studied in 2. The effects of the intramuscular injection of 0.01 mg. of epinephrine hydrochloride per kilogram of body weight were studied in 44 patients, with various diagnoses, in 23 of whom the response to epinephrine was studied again after treatment (Charts 1, 2, 3, 4, and 5).

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1. Bruce, L. C., and Peebles, A. S. M.: Quantitative and Qualitative Leucocyte Counts in Various Forms of Mental Disease, J. Ment. Sc. **50**:409, 1904. McDowall, C. F. F.: Leucocytosis: Its Relation to, and Significance in, Acute Mental Disorders, ibid. **54**:669, 1908; The Leucocyte and the Acute Insanities: An Epitome of Clinical Observations, ibid. **55**:726, 1909.

2. Rud, F.: The Eosinophil Count in Health and in Mental Disease: Biometrical Study, Acta psychiat. et neurol., Supp. 40, 1947.

3. Graziani, A.: Richerche sulle modificazioni citologiche del sangue nelle principali psicosi, Riv. sper. di freniat. **36**:878, 1910.

4. Altschule, M. D., and Parkhurst, B. H.: Decreases in Blood Eosinophilic Leukocytes After Electrically Induced Convulsions in Man, J. Clin. Endocrinol. **9**:440, 1949.

OBSERVATIONS

Blood Eosinophil Count.—Eosinophil counts were in or below the low normal range in the majority of patients studied. The mood, degree of activity, and nutritional status did not affect the cell count, and the type of mental disease had little influence (Table 1; Chart 1). Patients who had been ill continuously for more than six months to a year had counts below 100 per cubic millimeter of blood less frequently than those in whom the mental disorders were of shorter duration.

Variation in Eosinophil Count.—The range of variation in cell counts obtained several days to a week apart shortly after admission and before treatment usually

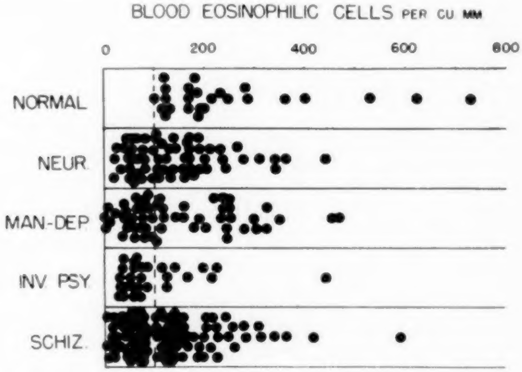

Chart 1.—Eosinophil counts on venous blood in various conditions before treatment.

TABLE 1.—*Eosinophils per Cubic Mm. of Blood*

Diagnosis	Number of Cases	Percentage of Counts: Below 100/Cu. Mm.	Percentage of Counts: Below 200/Cu. Mm.
Normal	25	0	56
Neurosis	59	21	78
Manic-depressive psychosis	58	48	69
Schizophrenia	97	44	80
Involutional psychosis	28	68	89

was within ±25% (Table 2). In five instances the second count was much lower than the first; in two of these the patient's condition was visibly worse at the time of the second count (Table 2), whereas in the others (Table 2) lowering of the eosinophil count was found 1½ to 6 hours before the patients' psychosis suddenly became exacerbated. In one instance (Table 2) the second count was much higher than the first; the patient had improved in the interval.

The effect of complicating allergic disorders was to cause increases in the eosinophil count even when the overt manifestations of allergic reactions were minimal or absent (Table 3).

Effect of Epinephrine.—Of 44 untreated patients studied before and again four hours after the intramuscular injection of 0.01 mg. of epinephrine hydrochloride per

kilogram of body weight, 35 showed decreases of 50% or more in the eosinophil count (Chart 2); 7 of 28 schizophrenic patients, 1 of 5 manic-depressive patients, and 1 of 10 neurotic patients showed decreases of less than 50% in the eosinophil count after the injection of epinephrine (Chart 2). The percentage of the decrease in blood eosinophils after four hours paralleled that of the increase in the blood sugar level in the first hour after injection of epinephrine when allowance was

TABLE 2.—*Average Deviation of Eosinophil Counts Three to Seven Days Apart*

	Number of Patients	
Average Deviation, %	Steady Clinical State	Changing Clinical State
± 0- 5	5	0
± 6-10	9	0
± 11-15	4	0
± 16-20	5	0
± 21-25	3	0
± 26-30	0	0
± 31-35	0	2
± 36-40	0	1
± 41-45	0	0
± 46-50	0	1
± 51-55	0	2

TABLE 3.—*Relation of Eosinophil Count to Allergic State*

Patient	Cell Count, Cu. Mm.	Comment
W	391	July 1950: psychotic
	765	Later: mild hay fever
	382	August 1950: remission
	340	Summer 1951: psychotic relapse
Ro	288	Food allergy
	119	Allergy improved with diet; psychosis in remission
Ra	127	Psychotic
	3,569	Reaction to penicillin
	413	Six wk. later: psychosis improved
P	50	February 1951: psychotic
	141	May 1951: remission
	259	Summer 1951: hay fever; psychosis in relapse

made for seasonal variations in the glycemic response to epinephrine (Chart 3). One schizophrenic patient in whom no fall in eosinophilic cells occurred after the intramuscular injection of 0.4 mg. of epinephrine hydrochloride showed a fall of 100% after intramuscular injection of 25 mg. of corticotropin. After treatment with insulin or electroshock or both, the eosinophilic response to epinephrine was not significantly changed in 19 of 23 patients (Chart 4); significantly greater responses occurred after treatment in 2 schizophrenic patients, and significantly decreased responses in 2 others with schizophrenia (Chart 4).

Effect of Pregnancy.—Two psychotic patients were studied late in pregnancy. For one, observed from three weeks until four days before term, five eosinophil

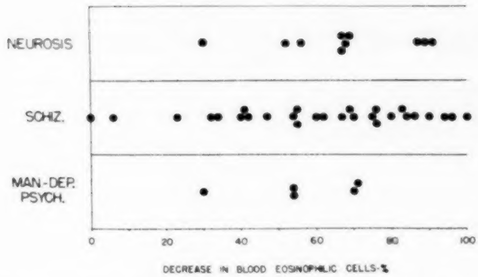

Chart 2.—Effect of epinephrine hydrochloride (0.01 mg. per kilogram of body weight, injected intramuscularly) on the eosinophil count in mental disorders.

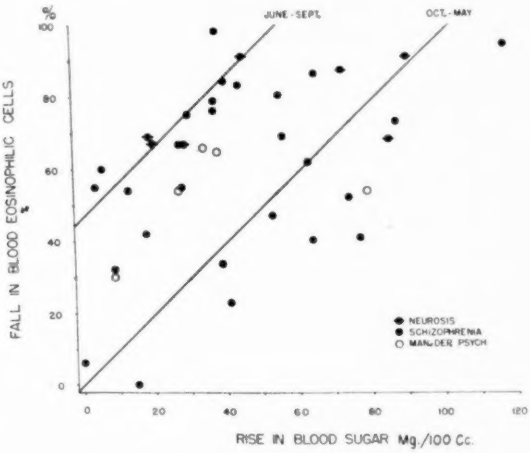

Chart 3.—Relation of the fall in blood eosinophils to the rise in blood sugar after injection of epinephrine.

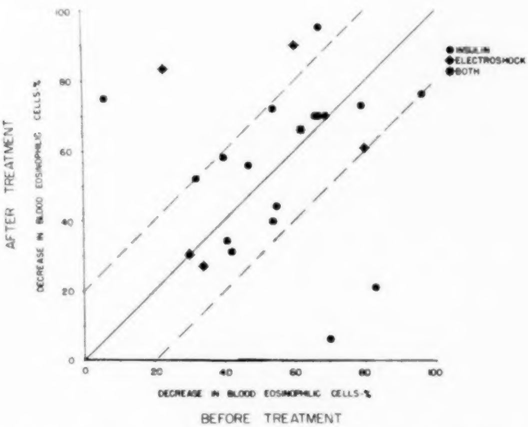

Chart 4.—Effect of treatment on the eosinopenic response to the intramuscular injection of epinephrine hydrochloride (0.01 mg. per kilogram). The points lying above the diagonal line indicate an increase in the degree of eosinopenia after treatment, and those lying below it indicate a decrease; the broken lines enclose the range of spontaneous variation.

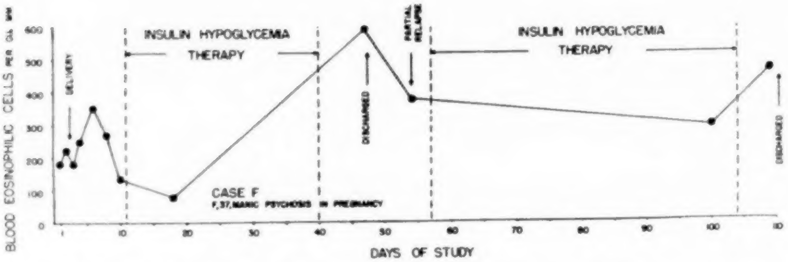

Chart 5.—Blood eosinophil counts in a case of manic psychosis commencing in pregnancy.

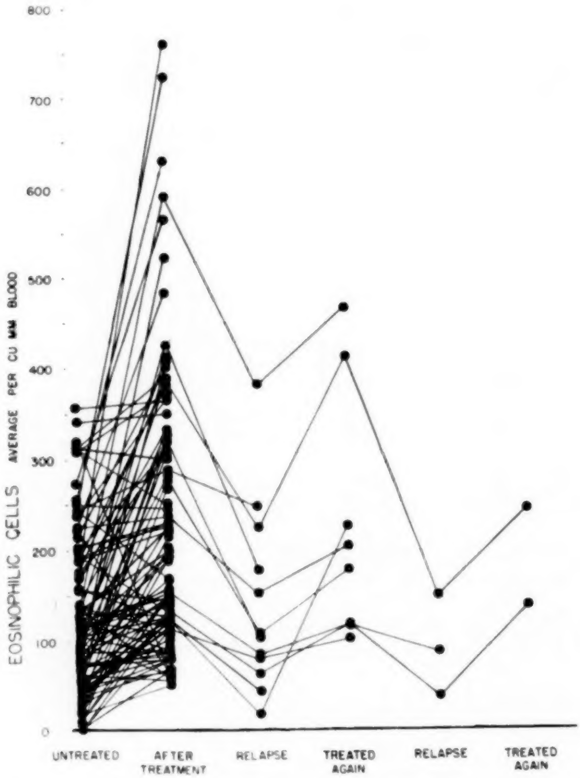

Chart 6.—Effects of treatment and of relapse on blood eosinophil counts.

counts ranged from 25 to 150 per cubic millimeter, with an average of 80. For the other (Chart 5), the counts also were normal for pregnancy, rose after delivery as the psychosis improved, and fell with exacerbation of the psychosis.

Effect of Treatment.—Blood eosinophil counts made not less than five days after the end of a course of ambulatory insulin or electroshock treatment were compared with those made before treatment; a significant change was considered to have occurred when the counts made before and after treatment differed from their mean by more than ±30%. This is an extremely rigorous test of significance. Significant increases in eosinophilic cells occurred in 53% and smaller changes in 38% of the patients whose condition improved (Charts 6 and 7). Significant increases did not occur in patients whose condition was not improved after treatment (Chart 7). In addition, patients not represented in Chart 5 showed changes in the eosino-

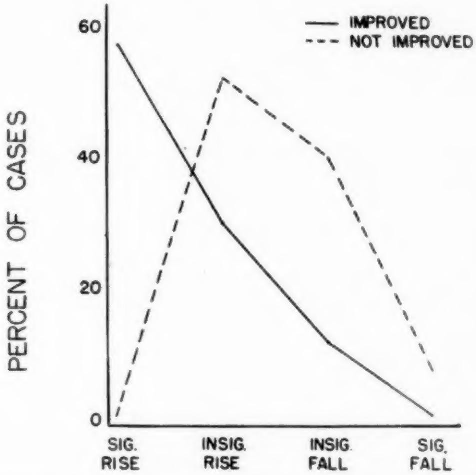

Chart 7.—Percentage of patients with improvement and of patients without improvement after treatment who showed changes (*Sig. rise; insig. rise; insig. fall; sig. fall*) in the blood eosinophil count.

phil count that were opposite in direction to that expected. One of them (W, Table 3) showed a fall of from 765 to 382 per cubic millimeter, even though she showed improvement; she had had hay fever at the time of the first count. Another patient (RO) showed a decrease of from 288 to 119 eosinophils per cubic millimeter, associated with improvement; she had had food allergy at the time of the first count. The third (Ra, Table 3) showed a fall of from 3,569 to 413 eosinophils per cubic millimeter of blood, with improvement in the psychosis; the high count had been associated with an allergic reaction to penicillin.

COMMENT

The common finding of low blood eosinophil counts in patients with untreated mental disease corroborates the observations of workers of half a century ago.[1] The changes found in 12 patients of the present series, each of whom was studied here

during psychotic episodes, after recovery from them, and in a total of 15 subsequent readmissions to the hospital in relapse, suggest that even when the number of blood eosinophils is in the normal range the count is lower during the psychosis than when the patient is well (Chart 6). Marked decreases in eosinophil counts seen in three untreated patients just before spontaneous exacerbation of the illness are of particular interest in this regard. The usual finding of normal blood eosinophil counts in patients who had been ill with mental disease continuously for several years is consistent with what is known of the tendency of blood eosinophils to rise after an initial fall in patients given corticotropin for long periods for the treatment of various diseases.

The finding of low blood eosinophil counts largely in patients in whom the illness was of relatively recent onset impairs the value of the cell count as a diagnostic test.

It was shown previously that shock treatments were followed after four hours by marked decreases in blood eosinophil counts,[4] that the blood eosinophil counts between treatments were lower than those in the untreated patient,[4] and that the decreases caused by each shock treatment became less and less marked as treatments increased in number.[5] A subsequent increase in the eosinophil count above the initial level usually was associated with improvement (Charts 6 and 7). The finding of a rise in the eosinophil count in patients who showed improvement after treatment corroborated observations made by other investigators in the past.[6] On the contrary, decreases in the cell count persisting after the end of treatment in the present study were associated with no improvement (Chart 7). In patients receiving electroshock treatments and in whom the development of confusion gives a semblance of remission of the psychosis, a decrease in eosinophils maintained after the end of the course of treatment is one indication for the resumption of therapy. Use of the eosinophil count for purposes of estimating the effectiveness of shock therapy is, however, subject to several limitations; improvement that is only slight or of short duration, i. e., several weeks, is associated with changes that are similar to those seen in patients with pronounced and lasting improvement. In addition, other influences may by themselves affect the eosinophil count. The influence of allergy phenomena is shown in patients studied here (Table 3); high counts, misleading in regard to the patient's clinical state, may be caused by allergic states. Low counts that do not reflect accurately the clinical state are commoner and may be caused by trauma, febrile diseases,[7] or even passing emotional upsets.

5. Altschule, M. D., and Parkhurst, B. H.: Effect of Treatment on Excretion of 17-Ketosteroids in Patients with Mental Disease, Arch. Neurol. & Psychiat. **64**:516 (Oct.) 1950.

6. Footnote 1. Jackson, D. J.: The Clinical Value and Significance of Leucocytosis, J. Ment. Sc. **60**:57, 1914. Itten, W: Zur Kenntnis hämatologischer Befunde bei einigen Psychosen, Ztschr. ges. Neurol. u. Psychiat. **24**:341, 1914. Kahlmeter, G.: Blutuntersuchungen bei einem Fall von Dementia praecox mit periodischem Verlauf, ibid. **24**:483, 1914. von Leupoldt, C.: Blutbilder bei Geisteskranken, Arch. Psychiat. **75**:271, 1925; Blutbilder bei Geisteskranken: I, ibid. **82**:669, 1928. Lehmann, H. E.; Turski, M., and Cleghorn, R. A.: The Eosinophil Response to ACTH in the Manic Phase of the Manic-Depressive Psychosis, Canad. M. A. J. **63**:325, 1950. Sackler, R. R.; Sackler, M. D.; Sackler, A. M.; Greenberg, D.; van Ophuijsen, J. H. W., and Tui, C.: Eosinophile Levels in Hospitalized Psychotics During Combined Testosterone-Estrogen Therapy, Proc. Soc. Exper. Biol. & Med. **76**:226, 1951.

7. Altschule, M. D.; Parkhurst, B. H., and Promisel, E.: Effects of Intravenous Injection of Typhoid Vaccine on Blood Leukocytes and Adrenal Cortex, Arch. Int. Med. **86**:505 (Oct.) 1950.

Observations made in an earlier study[8] do not support the concept that the adrenal gland in patients with mental disease is less responsive than normal to the effects of corticotropin, for all patients studied showed normal decreases in the eosinophil count after the injection of the hormone. It is possible that the abnormally slight decreases in blood eosinophils in some psychotic patients after the injection of epinephrine may indicate a defect in the anterior lobe of the pituitary gland or in hypothalamic centers that regulate its activity. An alternative explanation, however, is suggested by the observation that such patients also exhibit diminished glycemic responses in the first hour after the injection of epinephrine (Chart 3); a decrease in the amount of change in two phenomena effected by entirely different mechanisms suggests that in such patients the inactivation of injected epinephrine in the tissues may proceed at an abnormally rapid rate.[9] Other authors have shown that debilitated patients or those ill with one of a wide variety of bodily ailments may show decreased eosinopenic reactions to epinephrine.[10] It should be noted that Jacobowsky, in 1924,[11] observed that schizophrenic patients show eosinopenia after injection of epinephrine and that Bliss and associates[12] found that schizophrenic patients show normal eosinopenic responses to epinephrine when the latter is given dissolved in oil.

The eosinophil count late in normal pregnancy is low in the normal range, falls sharply at term, and returns to normal by the third day post partum, remaining at that level thereafter.[13] The eosinophil counts in the two psychotic pregnant women studied here were in the range described by others[13] for nonpsychotic pregnant women. In one patient delivered of her infant here, the normal rise in the eosinophil count occurred post partum and was associated with improvement in her mental state; a few days later, however, exacerbation of the psychosis occurred, and the blood eosinophil count fell.

The observations in the present study are consistent with the concept that severe neuroses and schizophrenic, manic-depressive, and involutional phychoses are associated with an increase in some adrenocortical functions and that recovery is associated with depression of these functions. No valid answer can be given at present to the question whether the changes found are consequent to the disease or are indicative of the activity of a factor that is the cause of the mental disease.

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8. Altschule, M. D.; Promisel, E.; Parkhurst, B. H., and Grunebaum, H.: Effects of ACTH in Patients with Mental Disease, Arch. Neurol. & Psychiat. **64**:641 (Nov.) 1950.

9. Altschule, M. D., and Siegel, E. P.: Inadequacy of the Glycemic Reaction to Epinephrine as a Measure of Hepatic Glycogen, Am. J. M. Sc., to be published.

10. Guest, C. M.; Kammer, W. H.; Cecil, R. L., and Berson, S. A.: Epinephrine, Pregnenolone and Testosterone in Treatment of Rheumatoid Arthritis, J. A. M. A. **143**:338 (May 27) 1950. Solomon, D. H., and Shock, N. W.: Studies of Adrenal Cortical and Anterior Pituitary Function in Elderly Men, J. Geront. **5**:302, 1950. Brenner, L. O.; Waife, S. O., and Wohl, M. G.: The Eosinophile Response in Chronic Disease and Malnutrition, J. Lab. & Clin. Med. **37**:593, 1951. Perlmutter, M., and Mufson, M.: The Hypoglycemic and Eosinopenic Response to Insulin: A Test for Pituitary-Adrenal Insufficiency, J. Clin. Endocrinol. **11**:277, 1951.

11. Jacobowsky, B.: Untersuchungen über die Senkungsgeschwindigkeit der roten Blutkörperchen bei der Dementia praecox, Upsala läkaref. förh. **30**:227, 1924.

12. Bliss, E. L.; Rubin, S., and Gilbert, T.: The Effect of Adrenalin on Adrenal Cortical Function, J. Clin. Endocrinol. **11**:46, 1951.

13. Davis, M. E., and Hulit, B. E.: Changes in Circulating Eosinophils in Women During the Menstrual Cycle and Reproduction, J. Clin. Endocrinol. **9**:714, 1949.

There is ample evidence that emotional upset causes eosinopenia in normal man [14]; even mental concentration that is not overtly emotionally charged may have this effect. In the present study, however, eosinopenia was found in apathetic or outwardly happy, confident psychotic patients, as well as in those who were agitated, tense, depressed, frightened, or maniacal; moreover, in several instances a fall in eosinophil count preceded exacerbation of the psychosis. It is impossible to state whether or not unconsciously perceived stresses were responsible for the eosinopenia that was found in patients not overtly upset. Nevertheless, the fact that adrenocortical hormones of the types that produce eosinopenia may cause a psychosis in normal subjects or may exacerbate the disease in those already psychotic suggests that the hyperactivity of the adrenal cortex found in patients with some types of mental disease is a causal factor, at least in the maintaining of the mental disorder.

SUMMARY AND CONCLUSIONS

The eosinophil count of venous blood is usually low in patients with severe neuroses or with manic-depressive, involutional, or schizophrenic psychoses; when these conditions are of long duration, the counts are less likely to be low.

After treatment with ambulatory insulin or electroshock therapy, the count usually rises in patients who show improvement and usually changes insignificantly in patients who do not. Several sources of error prevent the use of the blood eosinophil count as a diagnostic aid or as an indicator of the adequacy of shock treatment.

The eosinopenic response to epinephrine in the patients with mental disorders studied here is similar to that found in many other chronic illnesses; treatment has no consistent effect upon this reaction.

The significance of the findings in relation to the problem of adrenocortical function in mental disease is discussed.

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THE CEREBELLAR HEMANGIOBLASTOMAS

Review of Fifty-Three Cases, with Special Reference to Cerebellar Cysts and the Association of Polycythemia

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CUSHING AND BAILEY[1] believed that xanthochromic cysts of the cerebellum which were not definitely associated with gliomas were in all likelihood of hemangioblastomatous origin. Our experience with those cerebellar cysts led us to analyze our material of the past 20 years, chiefly in order to establish their relation to the hemangioblastomas. We also wished to determine the incidence of multiple hemangioblastoma, i. e., Lindau's disease, in our series and to examine the occurrence of polycythemia in patients with hemangioblastoma.

CASE MATERIAL

This study comprises 48 surgically verified cases of cerebellar hemangioblastoma or hemangioblastomatous cyst and 5 cases in which the tumor was first disclosed at autopsy. Thirty-seven occurred in the Neurological Institute of New York between 1929 and 1949, and 11, in the Veterans Administration Hospital, New York. A total of 32 hemangioblastomas were verified cytologically, and 7 were verified by inspection at operation. Included in this study are nine cases of large cerebellar cysts in which the cytologic verification of hemangioblastoma could not be made. The latter are considered to be of hemangioblastomatous origin, for reasons which will be brought forth later.

The analyses of our data were made according to the gross characteristics of the tumors, which were divided into three main categories: "solid," "solid with cysts," and "cysts." This division was made on the basis of clinical interest in the possible specificity of symptoms created by these various forms, as well as in determining the factors which each of these types exercised in the over-all course of the illness and the surgical results.

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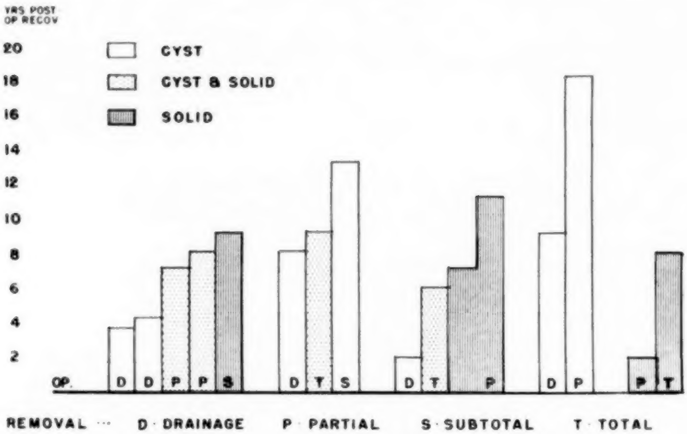

Chart 1.—In the first surgical period, from 1924 to 1934, five patients had operations, and all were operated on subsequently for recurrences. The average period of freedom from severe symptoms following the first operation was 6.7 years. One patient had a cyst emptied only, with a total survival period of 19 years, the periods being 10 and 9 years, respectively, for the two operations. For four patients with histologic verification of the tumor, the average period of freedom following the first operation was 4.5 years, the longest being 9.5 and the shortest 1.5 years. The average period of freedom following each subsequent operation was 3.4 years.

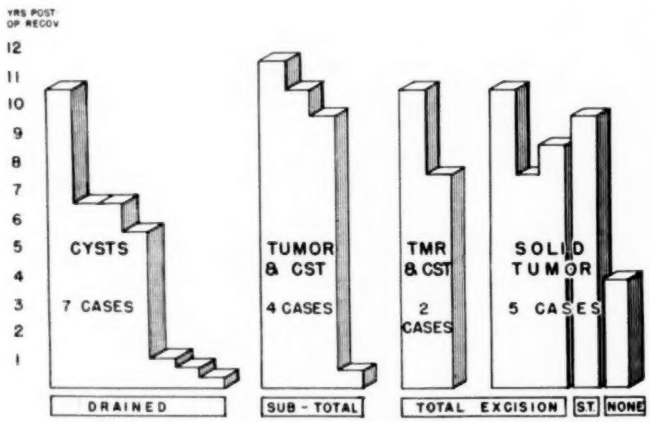

Chart 2.—In the second surgical period, from 1935 to 1944, inclusive, 18 patients had operations. In all cases in which cysts were found, they were opened and drained. In seven cases of cysts there was no removal of the walls of the cyst, or only partial removal, and in one case of solid tumor there was only partial removal. The average period of freedom from symptoms was 4.9 years in the case of cyst and 4.8 years in the case of a solid tumor.

Total removal was reported in two cases of cystic tumor and in two of solid tumor. The average period of postoperative freedom was 9.5 years for the cysts and 8.5 years for the solid tumors.

Thus, the duration of freedom from symptoms when there has been a subtotal or total removal of the cyst wall is almost the same as that for subtotal or total removal of a mural nodule. This period is about twice that which follows simple drainage of the cyst and decompression of the tumor without total excision.

TABLE 1.—*Case Incidence of Cerebellar Hemangioblastomas*

Surgically verified	
Cytological confirmation	32
Verified by inspection at operation	7
Cysts only, without solid tumor	9
Total	48
Found at autopsy only	5
Total	53

TABLE 2.—*Surgical Cases of Cerebellar Hemangioblastomas*

Type of Tumor	Age, Yr. at Onset of Symptoms		1-10		11-20		21-30		31-40		41-50		51-60		Total
	Youngest	Oldest	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	
Solid	20	55	..	...	..	...	3	6.2	3	6.2	5	10.4	3	6.2	14
Solid and cystic	17	50	1	2.0	3	6.2	7	14.5	9	18.7	5	10.4	..	...	25
Cysts	4	60	1	2.0	..	...	4	8.3	2	4.1	1	2.0	1	2.0	9
Total (cases)			2		3		14		14		11		4		48
Per cent				4.0		6.2		29.3		29.3		22.9		8.2	100%
Average, 31 years															

TABLE 3.—*Symptoms Leading to Operation in Cases of Cerebellar Hemangioblastomas*

	Solid Tumors	Solid and Cystic Tumors	Cysts	No.	Percentage
A. Initial symptom					
Headache	14	24	6	44	91.6
Cerebellar, brain stem	..	..	3	3	6.3
Blindness	..	1	..	1	2.1
B. Papilledema, D.					
6	..	4	..		
5	1	1	..		
4	1	1	..		
3	3	1	2		
2	2	4	..		
1	5	10	5		
				40	84.0
None	2	4	2	8	16.0
C. Cerebellar signs					
Ataxia	8	19	9	36	75.0
Adiadochokinesia	12	16	5	33	69.3
Romberg sign	6	20	6	32	67.2
Nystagmus	5	10	5	20	42.0
Dysmetria	4	7	6	17	35.7
D. Vomiting					
With papilledema	6	15	6	27	56.7
Without papilledema	1	..	1	2	4.2
					60.9
E. Brain stem and cranial nerves (diplopia and long-sensorimotor-tract signs)	8	13	7	..	58.8
Vertigo	6	17	2	25	52.5
Tinnitus	4	4	0	8	16.8
Caloric responses					
Performed	4	15	2	21	
Normal	3	9	2	14	66.6
Decrease					
Ipsilateral	1	2	..	3	14.5
Contralateral	..	1	..	1	4.7
Bilateral	..	2	..	2	9.4

GENERAL CLINICAL STATISTICS

Age at Onset of Symptoms.—The earliest onset of symptoms was at 4 years, and the latest, at 60 years of age. Both the patients had cysts only. The rest had the onset of symptoms between the ages of 17 and 56; of this group, 14 had solid tumors, and 25 had solid and cystic tumors. The distribution, in decades, was as follows: first decade, 4% ; second, 6.2% ; third, 29.3% ; fourth, 29.3% ; fifth, 22.9%, and sixth 8.2%. Thus, in 81.5% the onset occurred between the ages of 20 and 50, the average age being about 31.

Table 4.—*Duration of Symptoms Before Operation*

Type of Tumor	No. of Cases	Weeks						Months									Years								
		2	3	4	5	6	7	1	2	3	4	4.5	5	6	7	8	1	1.5	2	2.5	3	4	4.5	5	6
Solid (14 cases)...	1	..	..	..	..	..	..	X	X	X	..	X	X	X	..	X	..	X	X	..	..	X	..	..	..
	2	..	..	..	..	..	..	..	..	X	..	..	..	X	..	..	..	..	X	..	..	..	..	..	..
	3	..	..	..	..	..	..	..	..	X	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Solid and cystic (25 cases)	1	X	X	X	X	X	X	X	X	X	X	..	..	..	X	..	..	..	X	X	X	X	X	..	X
	2	X	X	..	..	..	..	..	..	X	..	..	..	..	..	..	..	..	X*	..	..	X	..	..	..
	3	X*	..	..	..	..	..	..	..	X	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
	4	..	..	..	..	..	..	..	..	X	..	..	..	..	..	..	..	..	..	..	..	..	..	..	..
Cysts (9 cases)..	1	X	..	..	..	..	X	..	X	X	..	..	..	X*	..	X	X	..	..	..	X	..	..	..	..
	2	..	..	..	..	..	..	..	..	..	..	..	..	X	..	..	..	..	..	..	..	..	..	..	..

* Mild symptoms for many years.

Table 5.—*Surgical Treatment of Cerebellar Hemangioblastomas*

A. Operations

	No. of Patients	No. of Operations	Post-operative Deaths	Mortality, %
Single-stage suboccipital craniectomy..................	36	36	3	8.3
Multiple-stage suboccipital craniectomy................	12	32	6	18.1
Total no. suboccipital craniectomies..............	48	69	9	13.1
Subtemporal decompression	1	1	1	
Total number of operations........................	49	70	10	14.0

B. Causes of Death

Uncontrollable hemorrhage from tumor..	2
Secondary hemorrhage, subdural, supratentorial...	1
Meningitis, acute suppurative, postoperative..	1
Invasion of medulla oblongata by tumor...	1
Direct compression of meaulla by tumor...	1
Irremovable vascular tumor; no benefit from decompression..........................	2

Sex.—Among the 42 patients at the Neurological Institute, the distribution between the sexes was almost equal, there being 19 females and 23 males. All the patients in the Veterans Administration Hospital were men, but since there are relatively few women veterans, this is of no general statistical importance.

SYMPTOMS LEADING TO OPERATION

Initial Symptoms.—Symptoms and signs of increased intracranial pressure predominated, and the initial symptom in 44 cases, or 91.6%, was headache. In three other cases the first symptoms recorded were of involvement of the cerebellum or brain stem, and in one case blindness developed insidiously. A specific relation between the location of the tumor and that of the headache was sought but

not found. Of cases of tumor in a cerebellar hemisphere, headache was nuchal or suboccipital in 23, and temporal or frontal in 21. Of seven cases in which the vermis was involved, the headache was nuchal or suboccipital in two and frontal or temporal in four. Headache was a more constant symptom in the cases of solid tumors, or of solid tumors with cysts, than in cases of cysts alone. Headache was the earliest symptom in 38 of 39 cases, or 97.3% of those in which the tumor was solid, whereas it occurred first in 6 of 9 cases of cyst, or in 66.6%.

Papilledema was found in the initial examination in 40 cases, or 84%, and was absent in the remainder. Cerebellar signs were third in frequency. Ataxia, adiadochokinesia, and unsteady stance were the predominant signs occurring in 75, 69.3, and 67.2% of the three categories, respectively. Nystagmus and dysmetria occurred in 42.0 and 35.0%, respectively.

Vomiting occurred in 29, or 60.4%, of the cases. In 27 of these, or 93.1% of cases with vomiting, there was papilledema, and in the remaining 2 cases there was none. In one of the latter the tumor presented into the fourth ventricle. The inference is that in most instances the vomiting was due to the effects of generalized increased intracranial pressure rather than to local irritation of the nuclei in the floor of the fourth ventricle.

Vertigo occurred in 25 cases. The tumor was hemispheral in 21 and in the vermis in 4. Vertigo was associated with 43% of the solid tumors, 68% of the solid and cystic tumors, and 22% of the cysts. Of patients with solid tumors, 4, or 25% of those who had vertigo, also had tinnitus; of the patients with solid and cystic tumors, 16% had both vertigo and tinnitus, and of the patients with cysts, vertigo occurred only twice in 22%, while tinnitus was absent.

Tinnitus was present in eight, or in 16.6%, of the cases. It was associated with vertigo in six and occurred twice without. In none of these cases was the tumor found to be involving the fourth ventricle, but other evidences of involvement of the brain stem and cranial nerves were present in four, or 50%, of the cases with vertigo.

Symptoms due to involvement of the long sensorimotor tracts and the cranial nerves and nuclei in the brain stem were present with 56.8% of the solid tumors, 52.0% of the solid and cystic tumors, and 77.0% of the cysts, an average of 58.8% for the entire group.

Caloric tests had been performed in only 21 cases and gave normal results in 66.6% of the cases in which they were made. In six cases the responses were decreased ipsilateral, and in two contralateral, to the tumor. In four cases they were reduced bilaterally.

SURGICAL RESULTS

Suboccipital craniectomies were performed in 48 cases. In 36 cases the operation was in a single stage and in 12 cases a total of 31 operations were performed. In two cases five operations were done; in one, four; in another, three, and in seven, two. One patient was too ill for ventriculography and definitive surgery and died after a subtemporal decompressive craniotomy. A total of 69 suboccipital craniectomies and a grand total of 70 operations were performed. The mortality for patients with a single-stage operation was 8.3%, and that for multiple-stage operations, 18.1%. The average mortality rate for the entire group of suboccipital craniectomies was 13.1%, and that for all operations was 14.0%.

The causes of death were as follows: uncontrollable hemorrhage from the tumor during and after operation; secondary (subdural) hemorrhage, supratentorial; acute suppurative postoperative meningitis; invasion of the medulla oblongata by tumor; direct compression of the medulla oblongata by tumor, tumor irremovable on account of vascularity, with no benefit from decompression. In one of the fatal cases the tumor was not attacked directly at the second (fatal) operation, but the tentorium cerebelli was split instead in an effort to afford a decompression.

Postoperative Survival Period.—The interval of time covered by this report readily falls into three surgical periods with respect to the surgical personnel of the Neurological Institute and to the general surgical technique and after-care of patients. Only the cases in the first two surgical periods, from 1924 to 1934, and from 1935 to 1944, inclusive, will be considered with respect to longevity and the period of freedom following the first operation.

SUMMARY OF CASES ILLUSTRATING OCCURRENCE OF MULTIPLE CEREBELLAR HEMANGIOBLASTOMATOUS LESIONS OF VARIOUS TYPES, ACCOUNTING FOR RECURRENT SYNDROMES OF COMPRESSION

CASE 1.—A man aged 35 had five cerebellar operations between March, 1924, and May, 1935, and one operation for trigeminal neuralgia in February, 1932. The total survival period following the first cerebellar operation was 11 years.

The first cerebellar operation was performed four months after the onset of bitemporal headache, nausea, vomiting, and weakness of the legs. Six cubic centimeters of yellow, non-coagulating fluid was aspirated from the left cerebellar hemisphere.

Five years later, in February, 1939, the cerebellum was tapped twice, percutaneously. Sixty cubic centimeters of straw-colored fluid was aspirated the first time, and one month later 12 cc. was removed.

In May, 1929, he underwent the second cerebellar operation. A cyst in the left cerebellar hemisphere was opened and drained, but no mural nodule was found. In October of the same year, another operation, performed because of persisting symptoms, disclosed numerous small cysts, degenerated cerebellum, and a reddish, plum-colored mass, "about the size of an olive," deep in the left cerebellar hemisphere. Profuse bleeding made possible only a biopsy, with the diagnosis of hemangioblastoma. In February, 1932, at which time there were no remarkable signs of cerebellar origin or of increased intracranial pressure, a posterior trigeminal rhizotomy was carried out by the subtemporal route, for trigeminal neuralgia.

One year later, in February, 1933, the fourth cerebellar operation, for relief of headache, papilledema, diplopia, and paresis of the hypoglossal nerve, revealed the left cerebellar hemisphere to be almost completely degenerated and cystic and to contain a tumor 2 by 2 cm. in diameter, which was removed subtotally. In May, 1935, the fifth suboccipital operation disclosed a large, very vascular tumor involving both cerebellar hemispheres and the vermis, and extending into the medulla and the spinal canal. The patient died nine days after operation, with hyperthermia and hiccups.

No roentgen therapy was given in this case. The total duration of the illness was 11 years and 5 months.

CASE 2.—*Five cerebellar operations—one for cerebellar cyst without tumor, one for recurrent solid and cystic and hemorrhagic hemangioblastomas; one for recurrent cyst and amorphous tissue, and two for solid hemangioblastoma. Survival, 4½ years.*

A man aged 22 was admitted to the Neurological Institute for operation five times between the onset of his illness, in February, 1939, and his death, in June, 1943, approximately 4½ years after the onset of illness. He received a total of 8,000 r of roentgen radiation between the first and fifth operations.

The first symptoms, occurring after a head trauma, were vertigo, for six weeks, and occipital headache, for three weeks. He had an ataxic gait, a positive Romberg sign, past-pointing,

dysmetria, adiadochokinesia, slurring speech, and nystagmus. The symptoms improved temporarily after each operation but recurred subsequently. The veins of the fundi were engorged, but there was never any true papilledema during his long illness.

At each of the five suboccipital craniectomies a new and different type of lesion was revealed, instead of a simple recurrence of the lesion disclosed at the previous operation.

The first lesion, observed in March, 1939, was a large cyst of the right cerebellum, 2 cm. below the surface, containing thick, xanthochromic fluid but no tumor or abnormal blood vessels. Anterior to the cyst wall was a small blood clot. The wall was composed of gliotic tissue.

Three months later there was an acute recurrence of headache and dizziness, which persisted. At the second operation, in October, 1939, six months after the first, instead of a recurrence of the cyst, we found the old cyst wall, which was collapsed and inert and contained no fluid. There were four new lesions: first, a small superficial cyst with xanthochromic fluid; second, a solid tumor of tenacious consistency, verified as a typical hemangioblastoma (this was subtotally removed); third, a large mass of tangled blood vessels, which caused profuse bleeding and could not be removed; fourth, a large solid and fluid blood clot, containing 60 cc. of fluid. It was the last lesion, apparently, which had precipitated the acute recurrence of symptoms three months previously.

At the third operation, in February, 1941, a large cyst, containing 10 cc. of thick, brownish fluid and stringy tissue, was found replacing the entire right cerebellar hemisphere. Cytologic examination of this specimen revealed no tumor cells, but merely amorphous material, fibrin, hemosiderin, and phagocytes. When this material was removed, the tentorium cerebelli and the lateral wall of the posterior fossa were completely exposed.

The fourth operation, in January, 1943, 23 months later, disclosed a new solid hemangioblastoma, which completely filled the former cavity in the right half of the subtentorial space.

The fifth operation, in June, 1943, revealed that the entire posterior fossa was filled with solid hemangioblastoma, a portion of which was removed. The patient died on the eighth postoperative day.

Case 3.—*Five operations; total survival period, 13.5 years. Large cerebellar cyst of vermis without tumor, drained 1933; small cerebellar cystic and solid hemangioblastoma, left hemisphere, removed in 1934; irremovable vascular tumor, superior surface of left cerebellum, recurrent 1941, 1942, and 1946.*

A man aged 30 first entered the Neurological Institute in May, 1933, and was operated on there in July, 1933, December, 1934, and November, 1941. He had two subsequent operations in other hospitals by another surgeon, in December, 1942, and October, 1946, when he died, 13 years after the first operation.

At the first operation, July, 1933, a large cyst containing coagulable fluid in the superior portion of the vermis was drained. No tumor was found. He continued to complain of headache and dizziness until after the second operation, in December, 1934, when a small superficial cyst, containing yellow fluid and a purplish tumor, 1.5 cm. in diameter, found in the left cerebellum was completely removed. This was verified as a hemangioblastoma.

Thereafter, he was free of symptoms and signs for six years, when headaches recurred for one year. At operation, in November, 1941, an extremely vascular tumor was encountered in the superior portion of the left cerebellar hemisphere. It could not be removed, but he again showed improvement after operation, except for weakness in the legs.

Headaches recurred in October, 1942. He then had another operation, in December, 1942, and a fifth in October, 1946, when he died. At the operation in 1942, which was technically very difficult, a large amount of tumor was removed, but there was little clinical improvement. At the last operation a gross digital removal of the very bloody tumor was performed. The patient died five hours after operation.

Case 4.—*Solid vascular cerebellar hemangioblastoma, right hemisphere; angioma, cauda equina.*

A white woman aged 28 had generalized headache of two months' duration, followed by nausea, vomiting, diplopia, and diminished vision. Examination revealed ataxia of gait, falling to the left on standing, bilateral paresis of the abducens nerve, bilateral diminished corneal response, and general weakness.

Operation, in January, 1933, revealed vascular adhesions between the cerebellum and the dura. An increased number of large blood vessels were present on the cerebellar surface, and the

right cerebellar tonsil was displaced downward through the foramen magnum. A tumor, measuring 2 by 2 cm., with average-sized varicose veins and arteries, was present in the inferior portion of the right cerebellar hemisphere. It was partially removed and proved to be a hemangioblastoma. The patient recovered uneventfully and was free from symptoms for two years.

In January, 1936, three years after the first operation, a secondary suboccipital operation was performed because of staggering gait, stiff neck, bulging suboccipital space, and failing vision, which had been severe for one month. A noncystic tumor, 3 by 5 cm., was totally removed from the right cerebellar hemisphere, where it lay in the right lateral floor of the posterior fossa. She again made an excellent recovery, took full charge of her household duties, and was free from symptoms until late in 1940, when she had lower back pain, followed by pain in the right leg, then the arm, and finally the hand and the back of the neck.

Reexamination revealed minimal residual cerebellar signs. Roentgenograms showed that silver clips from the cerebellar operation had become displaced into the cauda equina. Lumbar laminectomy in September, 1941, revealed an angioma involving the cauda equina. She did not recover satisfactorily and died in a sanatorium in July, 1942, of complications.

Roentgen therapy was given as follows: after the first operation (1933), 2,250 r; in 1934, 2,700; after the second operation, 2,800 r—a total of 7,830 r, all to the cerebellum; in 1941, 1,000 r to the lumbar and 700 r to the cervical region.

Freedom from intracranial symptoms followed the first operation for two years and the second operation, five years; the total survival after onset of symptoms was 9½ years.

Cysts Only

There were nine patients, or 17%, with xanthochromic cysts only. Three of these had two operations each for recurrence of symptoms of pressure following recovery from the first episode. The second operations were one, six, and eight years, respectively, after the first operation. Again, no tumor nodules were present within the walls of the cysts. Percutaneous drainage of the cyst for recurrent symptoms was done twice in two patients. Except for one of these two patients, who remains chronically ill, all these patients are well. The postoperative survival periods since the first operation are 5, 6, 9, 9, 10, 11, 13, 15, and 21 years, respectively.

The youngest patient in this group was 4 years of age, and the oldest, 60. Four were in the third decade of life, and three in the fourth decade. The average age was 31.

There was some difference in the incidence of symptoms in cases of cyst and those of solid tumor.

Headache was the first symptom in 100% of the cases of solid tumor and in 66.6% of cases of cyst. Signs of cerebellar, cranial-nerve and long-sensorimotor-tract origin were prominent in only 50% of the cases of solid tumor and in 75% of those of cyst. Vomiting occurred in 66.6% of cases of both types.

COMMENT

The cases summarized above were selected from the group with multiple-stage operations because they permit a cross-sectional view of different stages in the life history of the cystic cerebellar hemangioblastoma.

We have included the group of cysts without tumor because we believe them to be of hemangioblastomatous origin. This belief is based on the age incidence, the xanthochromic nature of the fluid, the similarity in the clinical findings to those in cases of tumor running a similar early course but later proved to be cystic hemangioblastoma, and the long, benign clinical course following drainage. We

believe that these cysts are not of gliomatous origin because of the older age group of the patients with cysts and because we have not had the same surgical experience in operating on the gliomas as we have in this group of multiple-stage operations.

Analyzing our observations in these cases of cerebellar hemangioblastoma, we find a number of definite clinical and pathologic trends. They follow two lines of growth potential: one toward solid and vascular masses, and the other toward cyst formation. Furthermore, they are multicentric within the cerebellum and posterior fossa, and these separate loci of new growth tend to develop into tumors in serial fashion. A tumor growing from any given locus may run its entire life course and become a cytologically inert cyst. It will not refill with fluid unless there remain angioblastic elements within its wall. These facts are illustrated in our Cases 2 and 3. Our observations are in line with those of Cushing and Bailey,[1] Perlmutter, Horrax, and Poppen,[2] and Raney and Courville.[3]

The recurrence of symptoms after a cyst which no longer contains a mural nodule of tumor is probably due to the growth of a second tumor. In our Case 2 the cyst encountered in the first operation, in which the wall of the cyst proper was not removed, remained inert and was seen at the second operation to resemble a flattened empty pouch. In Case 3 the first cyst occupied the vermis and did not refill, but a second cystic tumor grew in the left cerebellar hemisphere.

We have not been able to prove the cause of the formation of cysts. As in other cases of cyst-forming tumors, there is probably a combination of processes, consisting in part of plasmatic exudation from the abnormal blood vessels and in part of the liquefactive degeneration of the solid cellular tissue. In some cases hemorrhage, of greater or less degree, enters into the process. From Cumings'[4] chemical study of intracranial cysts of various types, it would seem that the plasmatic-exudation theory is most applicable in the case of hemangioblastomas. His analyses showed the contents to resemble blood plasma, with very little of the derivatives of cellular proteins, such as amino acid nitrogen, cholesterol and mucoprotein, substances which characterized the pituitary cyst and glioblastomatous cyst. On this basis, Cumings concluded it highly probable that diffusion of fluid from the blood caused these cerebellar cysts.

Hemorrhage into the tumor or cerebellum may be the cause of precipitate symptoms of recurrent pressure. In our Case 2 this was found to be true. In other cases the brownish color of the cystic fluid suggested that small hemorrhages had occurred. Globus[5] discussed two cases of hemorrhage into a cerebellar hemangioblastoma, and Wedd[6] reported another case of fatal spontaneous hemorrhage into a cerebellar hemangioblastoma. In these three cases there had been no

2. Perlmutter, I.; Horrax, G., and Poppen, J. L.: Cystic Hemangioblastomas of the Cerebellum: End Results in 25 Verified Cases, Surg., Gynec. & Obst. **91**:89-99, 1950.

3. Raney, R. B., and Courville, C. B.: Multiple Hemangioblastomas of the Central Nervous System: Review of Literature and Report of a Case, Bull. Los Angeles Neurol. Soc. **2**:104-114, 1937.

4. Cumings, J. N.: Chemistry of Cerebral Cysts, Brain **73**:244-250, 1950.

5. Globus, J. H.: Hemorrhage into Hemangiomatous Cerebellar Cyst, Arch. Neurol. & Psychiat. **64**:741-742 (Nov.) 1950.

6. Wedd, G.: A Fatal Case of Cerebellar Hæmangioma Without Previous Symptoms, with Note on Cerebellar Haemangiomata, J. Roy. Nav. M. Serv. **28**:185-188, 1942.

previous evidence of tumor. This was not true in our Case 2, however, in which the hemorrhage occurred three months after the first operation for a cyst.

In cases of more than one tumor it is likely that the first one will have the clinical and pathologic characteristics of cystic tumor, and the trend in later ones will be toward the solid and highly vascular type. It is in this type of tumor, and in the later stages, that polycythemia becomes manifest.

OCCURRENCE OF POLYCYTHEMIA

CASE 5.—*Autopsy findings illustrating occurrence of polycythemia and cerebellar hemangioblastoma.*

A white man aged 27 was admitted to the medical ward of the Presbyterian Hospital on May 16, 1937, complaining of frontal and occipital headache of three months' duration, followed by vertigo, ataxia, and blurred vision. He was incapacitated because of the headache, which had become much worse during the previous two weeks. His physician had made the diagnosis of brain tumor.

Examination revealed a husky, plethoric man, who was very tired and was suffering from severe headache. The temperature was 99 F., the pulse rate 96, the respiration rate 20, and the blood pressure 170 systolic and 140 diastolic. The heart was enlarged to the left. The spleen was not palpable. Positive neurologic findings were bilateral papilledema and severe hemorrhages; coarse, irregular nystagmus in lateral gaze; severe ataxia and inability to stand, and adiadochokinesia.

The cerebrospinal fluid was clear and colorless; it was under a pressure of 350 mm. of water with the patient in the recumbent position, contained 5 cells per cubic millimeter, and gave a positive reaction for globulin. There were 8,900,000 red blood cells, of normal size and shape; 9,300 white blood cells; a normal differential count, with no young forms, and a hemoglobin content of 150 mg. per 100 cc.

The vital capacity was 4,300 cc.; the venous pressure in the right arm, with the patient recumbent, was 83 mm. of water. The circulation time was 20 seconds after injection of 0.25 cc. of a 2% solution of sodium cyanide and 28 seconds after injection of 0.30 cc. In the phenolsulfonphthalein test, 30% of the dye (volume 500 cc.) was excreted in two hours. The specific gravity of whole blood was 1.0721. The estimated number of red blood cells, one hour after a meal and before phlebotomy, was 8,540,000.

Studies of the blood one hour after a meal gave the following values: potassium, 283.3 mg. per 100 cc. whole blood; cells, 366.0 mg. per 100 cc.; plasma, 17.2 mg. per 100 cc.; hematocrit reading, 72.7%; specific gravity of the plasma, 1.0290; protein content of plasma, 7.5 gm. per 100 cc.

On May 20, 1937, the carbon dioxide content of the serum was 66.9 vol. %, and the chlorides, expressed as sodium chloride, measured 583 mg. per 100 cc. The nonprotein nitrogen of the serum was 34 mg. per 100 cc., and that of whole blood, 44 mg. per 100 cc.; calcium measured 11.1 mg.; cholesterol, 247 mg., and bilirubin, 2 mg. per 100 cc., and phosphatase, 3.3 Bodansky units.

Despite frequent phlebotomies, with removal of 400 to 600 cc. of blood, the red blood cell count never fell below 6,000,000 or the hemoglobin below 104 mg. per 100 cc.

X-ray pictures of the skull revealed a thin, atrophic dorsum sellae and were interpreted as showing increased intracranial pressure.

The clinical diagnosis was polycythemia, which was causing increased intracranial pressure through multiple hemorrhages, thrombi, and secondary blockage of cerebrospinal-fluid absorption. The neurologist and the ophthalmologists also gave this interpretation of the symptoms and signs. No neurosurgical opinion was obtained. The clinical course was progressively poor, and he died July 8, 1937.

The pertinent autopsy findings are summarized as follows: Brain.—Internal hydrocephalus and flattening of the convolutions were evident.

Cerebellum.—Two large cysts were observed in the right cerebellar hemisphere, one containing a mural nodule of hemangioblastoma. The blood vessels were chiefly capillaries, of variable size, with some large, thin-walled sinuses and some arterioles. Microscopic examination showed that the intervascular tumor elements were elongated polygonal and irregularly rounded cells with long, oval nuclei and a moderate chromatin content. Some cells were coarsely vacuolated.

The cells were intimately associated with endothelial cells forming the linings of capillaries. A number of large cysts were lined with tumor cells and contained amorphous pink material. There were recent hemorrhages and no mitoses. A dense network of reticulin was present within and between the blood vessels. The walls of the cysts were composed of astrocytes and their fibers.

Spleen.—The spleen was entirely within the costal line. It was flabby; the pulp was friable, and there was no obvious fibrosis. Sections showed that the red pulp was diminished in amount and almost hemorrhagic in some regions. The Malpighian corpuscles were for the most part poorly defined and poor in lymphocytes but were normal in some areas. The intima of some arteries was thickened.

Liver.—The liver was just below the costal border. The capsule was normal, and the parenchyma was not congested. The liver cells were generally atrophic with rounding-off in some areas beneath the capsules. Some cells were vacuolated and contained a fine brown pigment. An occasional small island of hematopoiesis was seen.

Femoral Marrow.—There was no evidence of increased erythropoiesis. The marrow was normal.

Kidneys.—In the medulla of the lower pole of the left kidney was a brown-walled cyst, 1.5 cm. in diameter, with several cavities, separated by thin walls. These were lined with squamous to cuboidal epithelium. There was no unusual finding in the parenchyma to suggest primary or vascular disease.

Comment: This case is an instance of Lindau's disease, i. e., hemangioblastoma of the cerebellum with a (presumed hemangioblastomatous) cyst in the kidney, complicated by polycythemia vera.

The tumor of the posterior fossa was the cause of the principal symptoms, which were those of increased intracranial pressure and cerebellar compression, eventually causing the patient's death.

The symptoms of an expanding lesion were misinterpreted as arising from the severe polycythemia.

No cause of the polycythemia was disclosed at autopsy, except for occasional small islands of hematopoiesis in the liver.

Incidence of Polycythemia in Surgical Cases of Cerebellar Hemangioblastoma.—With 5,000,000 erythrocytes as the upper normal limit for women and 6,000,000 as the upper limit for men (Chart 3), preoperative erythrocyte counts in the cases of cysts revealed normal figures, ranging from 4,200,000 to 5,300,000 for both males and females. Preoperative erythrocyte counts in cases of tumor and cyst were made on 20 males and 6 females. The highest count for males was 5,700,000 and the lowest 4,300,000, both of which are considered within the normal range. For females the highest count was 5,100,000. With 5,000,000 as the upper normal limit, this count is 16% above normal.

Of the patients with solid tumor, six were males and four females. The highest red cell count for the males was 8,900,000 and the lowest 4,400,000. The highest count for the females was 5,400,000 and the lowest 4,100,000. If 6,000,000 is taken as the upper limit of normal for males, two patients, or 33.3%, had counts above this figure. If 5,000,000 is selected as the upper normal limit for females, one case, with a count of 5,400,000, represents 25% above normal.

If the entire 44 patients on whom blood cell counts were made is considered as a group, there were four patients, or 9.0%, with an initial preoperative count above the normal range. This represents an unquestionable trend toward polycythemia.

Of 11 patients, or 63.6%, who had recurrences, 7 showed a trend toward elevation of the erythrocyte count during the interval between the first operation and the subsequent ones. In two males, or 18.1%, this became a definite polycythemia. In two others the subsequent erythrocyte counts were 6,000,000 and 5,900,000, respectively, whereas the count before the first operation was normal. If these two counts are considered in the range selected by Carpenter, Schwartz, and Walker,[7] the incidence of polycythemia in this group with recurrences is 36.4%.

Comment on Polycythemia.—The association of polycythemia and disease in the nervous system is of both theoretical and practical importance to the neurologist and the neurosurgeon.

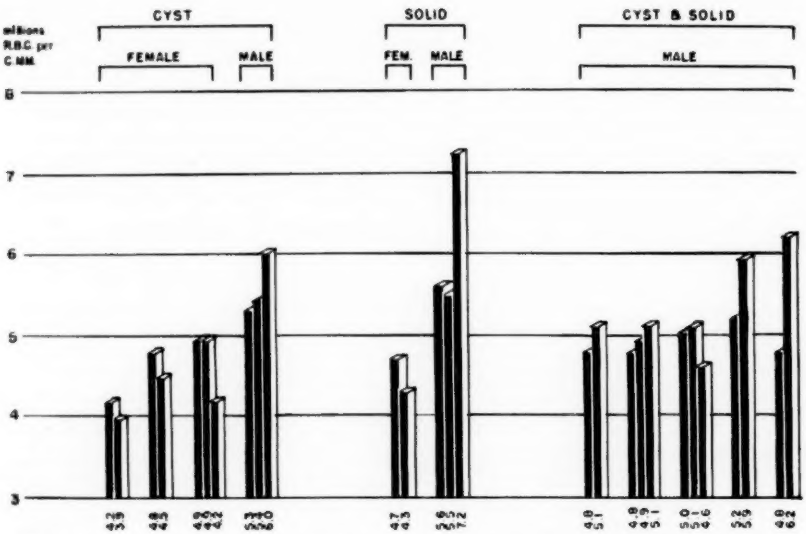

Chart 3.—Erythrocyte count in multiple operations for recurrence of cerebellar hemangiomas.

Polycythemia causes various nervous manifestations, and this subject was reviewed by Drew and Grant [8] in 1945. The particular problem which it poses to the neurosurgeon is the association of papilledema, thus making it imperative to rule out brain tumor. At the same time, it lies within the province of the neurosurgeon to attempt to determine the causal relation of these two conditions.

In any given case of true polycythemia, with an actual increase in erythrocytes, and not merely hemoconcentration, the polycythemia may theoretically originate in several ways. First, there may be dysfunction of the primary hematopoietic organs, i. e., the bone marrow. Second, there may be extramedullary erythropoietic germinal centers, e. g., in the liver and spleen. In our Case 5 there were hema-

7. Carpenter, G.; Schwartz, H., and Walker, A. E.: Neurogenic Polycythemia, Ann. Int. Med. **19**:470-481, 1943.

8. Drew, J. H., and Grant, F. C.: Polycythemia as a Neurosurgical Problem: Review, with Reports of 2 Cases, Arch. Neurol. & Psychiat. **54**:25-36 (July) 1945.

topoietic islands in the liver. Third, the polycythemia may be due to secondary stimulation of these centers by a disturbance of the oxygen balance in the circulating blood, due to arteriovenous shunts in the hemangioblastoma. Fourth, polycythemia may actually be produced or may accrue from erythropoiesis on the part of the hemangioblastoma itself. It is theoretically conceivable that the cerebellar hemangioblastomas may be erythropoietic.

Cushing and Bailey discussed this possibility in respect to the cavernous hemangioblastomas. They cited Sabin [9] and others [10] who have described this process in the embryonic cell masses from which the hemangioblastomas eventually are formed.

In various parts of the embryo, specifically in the area postrema of the fourth ventricle, the embryonic angioblasts differentiate from the mesoderm, and, after the formation of dense syncytia, plexuses of solid angioblastic cells form. Liquefaction then takes place within the cords, where there is a clear fluid plasma surrounded by endothelium. Some of the angioblasts become blood islands, and eventually generate erythrocytes.

However, Cushing and Bailey did not report the clinical occurrence of polycythemia in their cases, and they did not include the erythrocyte count in their published histories. In their fixed tissue preparations, they were unable to demonstrate definite evidence of formation of new blood in the vascular spaces of their tumors, but they stated that this might be due to the difficulty of identifying such elements in ordinary microscopic preparations. They did not conceive of the blood which was contained in the spaces of a cavernoma as being in actual circulation. However, they stated that, on the basis of the work of other investigators, evidence of hematopoiesis could be hypothesized in these tumors, as well as in the hemangioblastomas in other parts of the body.

In this respect, it seems significant to us that we encountered polycythemia only in those cases in which there was a solid or vascular tumor and in none of those in which there was a cyst only. However, in those cases of cyst in which there was a progressive change in the nature of the hemangioblastomas and subsequent operations revealed very vascular lesions, the polycythemia developed during this stage. This suggests a relation between the growth of new blood vessels and the presence of polycythemia.

Turner and Kernohan [11] noted that one of the outstanding features of the angiomas was the progressive enlargement of the individual blood vessels which go to form the mass of the tumor. To them this represented merely a hydrodynamic expansion, due to the inequality in the strength of the blood vessel relative to the force of the circulation. They did not discuss the presence or absence of clinical polycythemia, but they stated that there were no proofs of hematopoiesis in the fixed specimens.

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9. Sabin, F. R.: Preliminary Note on the Differentiation of Angioblasts and the Method by Which They Produce Blood-Vessels, Blood Plasma and Red Blood Cells as Seen in the Living Chick, Anat. Rec. **13**:199-205, 1917.

10. Pilliet, A. H.: Hématopoiesie dans les angiomes du foie, Progrès méd. **29**:50, 1891; cited by Cushing and Bailey.[1]

11. Turner, O. A., and Kernohan, J. W.: Vascular Malformations and Vascular Tumors Involving the Spinal Cord: A Pathologic Study of 46 Cases, Arch. Neurol. & Psychiat. **46**:444-463 (Sept.) 1941.

Carpenter, Schwartz, and Walker (1943)[7] and Walker[12] reported the association of cerebellar hemangioblastoma with polycythemia. They did not believe that the polycythemia was directly related to the type of tumor, because in 14 other cases of subtentorial hemangioblastoma this association did not exist. Furthermore, they noted that Cushing and Bailey had not mentioned it as a clinical observation in their monograph. Carpenter and associates and Walker hypothesized a neurogenic basis, by which the tumor stimulated hematopoietic mechanisms in the diencephalon. In support, they cited the work of Schafer in respect to sympathectomy in the control of polycythemia. Of their cases of cerebellar hemangioblastoma, polycythemia was present in 13.5%, and it was present in 18% of our surgical cases of hemangioblastoma. We do not believe that the polycythemia is specifically neurogenic, for we should then expect to find it as frequently with other types of cerebellar tumor. We are inclined to believe that there may be hematopoiesis in the hemangioblastomas themselves, although thus far we have no final proof that this is true.

However, because of the difficulty in determining this matter in ordinary fixed specimens, we decided to approach this aspect of the problem by way of tissue cultures. We have been fortunate in obtaining the interest and aid of Dr. Margaret Murray, in whose tissue-culture laboratory a specimen from one of our former patients was under study. The patient had his first cerebellar operation at the Neurological Institute in December, 1933. He had previously had a congenital "blood tumor" removed from his cheek. Headache, papilledema, and cerebellar ataxia were severe. There was no polycythemia. An angiomatous and irremovable tumor was observed in the left cerebellar hemisphere. He made a fairly good response to the decompression and was able to return to work for a time. Five courses of x-ray therapy were given him at the Neurological Institute between 1933 and 1946, at which time recurrent symptoms were severe. He was then admitted to Bellevue Hospital, and a second operation was performed, almost 17 years after the first. At this time he had severe polycythemia. Again, a very vascular tumor was found, and a specimen was furnished us for study through the courtesy of Dr. Wilfred Wingeback and Dr. Thomas Guthrie.

Dr. Murray[13] has given us the following report on the growth of the explant of tumor from this case: "In the earlier explants and transplants of the tumor there are numerous erythrocytes, but these are not in such numbers as to preclude their being viable mature red blood cells transferred from the tumor itself. However, there are a great number of free-lying nuclei among those erythrocytes which give the impression of being extruded. In only a few red blood cells are true nuclei apparent. Most of the erythrocytes are of the size of normal red cells, but in some areas they are larger and resemble erythroblasts." This single experiment is not conclusive as to the erythropoietic capacity of hemangioblastomas, but it is sufficiently suggestive to warrant further study in subsequent cases.

SUMMARY

1. The age of incidence of cerebellar hemangioblastoma in this series of 53 cases was from 4 to 60 years, with 8.5% between the ages of 20 and 50, the average age being 31.

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12. Walker, A. E.: Neurogenic Polycythemia: Report of a Case, Arch. Neurol. & Psychiat. **53**:251-253 (March) 1945.

13. Murray, M.: Personal communication to the authors.

2. The sex distribution was almost equal in the cases at the Neurological Institute, there being 23, or 54.8%, males and 19, or 45.2%, females. All patients in the Veterans Administration Hospital were men, but this is not of statistical significance in this study.

3. Von Hippel's syndrome, or angiomatosis retinae, was encountered definitely in one case and presumptively in another, an incidence of 3.6%.

4. Multiple cerebellar and extracerebellar hemangioblastomas, or Lindau's syndrome, occurred in five cases, an incidence of 10%.

5. Headache was the first symptom in 91.6% of the cases and was equally distributed in the suboccipital and the temporofrontal region. Signs of increased intracranial pressure predominated over localizing signs of cerebellar and brain-stem origin.

6. The postoperative period of freedom from symptoms was longest when all of the tumor or the wall of the cyst was removed.

7. The recurrence of symptoms following the complete drainage of a cyst without a mural nodule of tumor was proved in several cases to be due to the growth of new lesions, and not to the refilling of the old cysts.

8. In cases requiring multiple operations for recurrent symptoms, it was observed that the lesions found at the first surgical intervention were cystic and the subsequent ones were increasingly angiomatous.

9. Coincident with the trend toward greater vascularity in the recurring or newly formed hemangioblastomas, there was a tendency toward polycythemia. It was found in 18.0% of the entire series of surgical cases and in 63.6% of the group with multiple-stage operations for recurrence of very vascular tumors.

10. In tissue cultures of the surgical specimen in a case of recurrent vascular cerebellar hemangioblastoma, the explants contained many free-lying nuclei among the numerous erythrocytes, a few nucleated erythrocytes, and some apparent erythroblasts. It cannot be proved that the free-lying nuclei were extruded from the erythrocytes, but this possibility is entertained. It is concluded that this method of approach to the problem of polycythemia in cerebellar hemangioblastomas is worthy of further trial.

CONCLUSIONS

In relatively few of this series of cases, the stigmata were associated with the von Hippel-Lindau syndrome, and the incidence compares with that in Cushing and Bailey's series. There are sporadic reports of familial occurrence of presumed or proved instances of the von Hippel-Lindau syndrome. When such groups are included in larger series of surgical cases, they create an apparent discrepancy with the incidence reported in other large series, such as the present one and that of Cushing and Bailey.[1]

The degree of longevity and freedom from symptoms after operation is directly proportional to the degree of removal of the tumor and possibly, although not necessarily, to the degree of removal of the cyst wall.

The cerebellar hemangioblastomas arise from multicentric anlages. In many instances the recurrence of symptoms is unquestionably due to the growth of tumors other than those which first demanded surgical intervention. The recurrence of

symptoms after the complete evacuation of a cyst with no mural nodule and the finding of another cyst subsequently are probably due to the growth, degeneration, and/or exudation from vessels of another tumor, and not to the simple refilling of the first cyst.

The sudden recurrence of symptoms in the course of a hemangioblastoma should be considered a possible sign of acute hemorrhage into the cerebellum.

The association of polycythemia rubra with vascular tumors leads us to believe that the polycythemia may result directly from hematopoietic functions of these hemangioblastomas. However, it may represent merely a diathesis toward extramedullary erythropoiesis in the spleen and liver. Future observations on this type of tumor must include more extensive studies of the red blood cell relationships in the general circulation, as well as those within the hemangioblastomas themselves. Tissue cultures in one of our cases resulted in suggestive evidence of erythropoiesis, and this method warrants further investigation.

Abstracts from Current Literature

Edited by Dr. Bernard J. Alpers

Anatomy and Embryology

Further Studies on the Differentiation and Growth of Mauthner's Cell in Amblystoma. Jean Piatt, J. Exper. Zool. **113**:379 (March) 1950.

A variety of experiments were performed on Amblystoma embryos, ranging from stages 25 to 30, in order to study the effect on the growth and differentiation of Mauthner's cell. Most of the animals were fixed for sectioning in early feeding stages.

Mauthner's cell was present in the great majority of the animals in which vestibular and/or lateral-line roots were missing. Bilateral reduction of vestibular and lateral-line roots was no more efficacious in suppressing the development of the cell than unilateral reduction of the roots.

In two of eight animals in which the medulla had been temporarily isolated from the neural axis (five days in the flank region), Mauthner's cell was absent on one side. When present in these embryos, almost all the Mauthner cells were small and poorly formed.

Separation of the left and the right halves of the medulla by a tantalum-foil block (at stage 29) had no effect upon the normal differentiation of Mauthner's neuron, except that the axons remained ipsilateral in the spinal cord as far caudally as the sections were examined.

The results of these experiments, together with those of the previous work on Mauthner's cell, permit the author to present the hypothesis that the forces responsible for the initial differentiation of Mauthner's cell reside largely within the cell itself, but that the maintenance or full development of the neuron is dependent upon the presence of vestibular and lateral-line roots, and also upon its connection with intramedullary tracts.

Reid, New Brunswick, N. J.

Collateral Regeneration of Residual Motor Axons in Partially Denervated Muscles. Mac V. Edds Jr., J. Exper. Zool. **113**:517 (April) 1950.

The residual, intact motor nerve fibers in partially denervated muscles of the rat have been studied in gold-impregnated, teased preparations (Carey's method) and in sections after impregnation with silver (Bielschowsky's method). Three leg muscles (soleus, extensor digitorum longus, and tibialis anterior) and the anterior serratus muscle were studied at intervals from 1 to 43 weeks after permanent elimination of one of the spinal nerves (fourth lumbar and sixth cervical, respectively) which contribute to their innervation. The homonymous contralateral muscles served as controls.

The degree of denervation, which varied widely in the muscles studied, ranged from total to negligible in the different regions of the anterior serratus muscles. (Denervation was almost complete in the cephalic slips, and almost absent in the most caudal slips, of the anterior serratus muscles.) Hence, the residual intramuscular axons were interspersed with a variable number of aneuritic neurilemmal sheaths.

During the second postoperative week, the residual motor nerve fibers began to form fine collateral sprouts, which established contact with adjacent empty sheaths and were thus guided to denervated motor end-plates. Although the sprouting was maximal during the first month, it continued sporadically, at least through the fourth month. Most of the collateral branches became connected with end-plates, but the recovery of the latter required two to three additional weeks. Frequently, the sprouts which acquired terminal connections attained calibers within the normal range by the eighth postoperative week, but even in the oldest many new branches remained undersized.

All collateral sprouts arose within 1 mm. of the termination of the parent fibers. While some new branches originated at or near nodes of Ranvier, others appear to have arisen in internodal regions. It is unknown just how the penetration of the myelin sheath was effected.

A quantitative study, based on counts of nerve fibers and associated end-plates (terminal innervation ratio), established a direct correlation between the degree of original denervation and the number of new sprouts which were produced. In the severely paretic cephalic slips of the anterior serratus muscle, collateral branches were more than twice as numerous as in the caudal regions, where denervation of the muscle slips was moderate. On the average, the original terminal branches of the residual axons came to support almost three times the normal number of end-plates. In exceptional instances, as many as 30 times the normal number were connected with an old terminal fiber.

Evidence from this and previous experiments concerning the mechanism of collateral regeneration suggests that a local reaction between the terminal portions of intact fibers and the proliferating sheath cells of adjacent, interrupted fibers may constitute the necessary stimulus.

Edds concludes that the close correlation between the present results and previous physiological observations provides compelling evidence that the functional recovery of partially denervated muscles is due to the expansion of residual motor units.

Reid, New Brunswick, N. J.

The Development of Cholinesterase in the Central Nervous System of Amblystoma Punctatum. E. J. Boell and S. C. Shen, J. Exper. Zool. **113**:583 (April) 1950.

The normal development of cholinesterase in various regions of the central nervous system was studied in the larvae (stages 28 to 46) of Amblystoma punctatum. The cholinesterase activity, which was determined by the Cartesian diver technique, was related to the total nitrogen content of the tissue. In many cases the respiratory activity of the piece of nerve tissue was also measured.

The experiments demonstrated that the cholinesterase of the nervous system of such larvae is of the same type as that found in the nervous systems of various adult forms.

The first appearance of cholinesterase in the spinal cord coincided with the ability of the embryo to respond neurogenically to tactile stimuli (stage 36). No cholinesterase was detected in hindbrain, midbrain, or forebrain at this time. At subsequent stages the enzyme appeared in these regions of the central nervous system in sequence from posterior to anterior. In the hindbrain cholinesterase was first detected at stage 28; in the midbrain, at stage 39; and in the forebrain, at stage 42 +. In each region the course of increase of enzyme activity followed an approximately sigmoid curve between the time of its first appearance and the early feeding stages.

At all stages, the rate of increase and the ultimate level of enzyme activity was highest in the cord and was progressively lower in hindbrain, midbrain, and forebrain, respectively. On the other hand, the pattern of respiration, both its rate and its distribution in the various regions of the brain, was essentially constant during development.

Boell and Shen conclude that the increase in cholinestrase activity appears to be associated with functional differentiation, and not simply with increase in size of the various regions of the central nervous system.

Reid, New Brunswick, N. J.

An Experimental Analysis of Relations Between Parts of the Brachial Spinal Cord of the Embryonic Chick. Eleanor Lerner Wenger, J. Exper. Zool. **114**:51 (June) 1950.

In order to study the local intracentral factors involved in the development of the normal patterns of organization in the spinal cord of the embryonic chick, Wenger removed lateral halves, dorsal quarters, or dorsal halves of the neural tube at the brachial level of 15- to 25-somite embryos. A detailed study was made of 14 embryos so treated, ranging in age from 8 to 11 days of incubation.

Wenger concludes that short-range fibers play a negligible role in the development of the normal pattern of the mantle. The normal number of lateral motor cells developed in the absence

of the lateral half, the dorsal quarter, and probably also the dorsal half, of the cord. The lateral motor column developed normally in the absence of synaptic connections with commissural cells, and without at least some of the association cells. Since the entire mantle, as determined by area measurements, developed in the absence of the contralateral side of the cord, synaptic connections with commissural cells were unnecessary.

Wenger also concludes that interactions between adjacent parts of the mantle are negligible in the development of their normal patterns.

Wenger suggests that at the time of operation the neural epithelium constitutes a mosaic with many independent neural epithelial units. These are as follows: the ventralmost basal plate, which gives rise to the cells between the mesial motor column and the floor plate; the ventrolateral basal plate, from which the mesial motor column arises; the lateral basal plate, the source of the lateral motor column; the dorsal basal plate, which gives rise to internuncial cells; the alar plate, from which arise sensory horn cells and internuncial cells, and the roof, and probably also the floor, plate.

REID, New Brunswick, N. J.

NUTRITIONAL REQUIREMENTS OF THE EARLY CHICK EMBRYO: II. DIFFERENTIAL NUTRIENT REQUIREMENTS FOR MORPHOGENESIS AND DIFFERENTIATION OF THE HEART AND BRAIN. NELSON T. SPRATT JR., J. Exper. Zool. **114**:375 (July) 1950.

Explanation of blastoderms (the primitive-streak through the 5-somite stage) to various synthetic nutrient media was used as a method of studying the metabolic mechanisms underlying the processes of morphogenesis and differentiation of tissues and organs. By explanting embryos on a non-nutrient (buffered Ringer) medium, or on different quantities and kinds of substrates (glucose, mannose, fructose, galactose, sodium pyruvate, and lactate), or by lowering the pH below 7.3, or by decreasing the oxygen tension around the explant, the author demonstrated both quantitative and qualitative differences in the carbohydrate requirements for formation of the heart, central nervous system, and ectodermal epithelial derivatives.

It was found that in the first two days of development morphogenesis and differentiation of the central nervous system were most dependent on the proper environmental conditions. Brain and neural tube will not develop at concentrations of sugar substrate which are quite adequate for formation and pulsation of the heart. Another indication that the nutritional differences characteristic of the adult heart and brain are present during their development is the greater sensitivity of brain formation to changes in pH and oxygen tension.

As a rule, morphogenetic processes (regression of the streak; formation and closing of the neural fold; formation of the "tail," notochord, head fold, flexion of the head, etc.) required less exogenous, carbohydrate nutrient than processes of differentiation (histogenesis of brain, optic vesicles, heart; formation of otocysts, somites, etc.).

Spratt discusses the possible significance of the procedure and the bearing of the results upon the nature of embryonic differentiation. Included in the discussion is the interpretation of differentiation in terms of the enzymatic components of cells. The possibility that there is a fundamental energetic difference between form-building activities, which appear to be energy-release mechanisms, and the tissue-building activities, which appear to be energy-consuming processes, is suggested.

REID, New Brunswick, N. J.

X-RAY INDUCED DEVELOPMENTAL ABNORMALITIES IN THE MOUSE AND THEIR USE IN THE ANALYSIS OF EMBRYOLOGICAL PATTERNS: I. EXTERNAL AND GROSS VISCERAL CHANGES, LIANE BRAUCH RUSSELL, J. Exper. Zool. **114**:545 (Aug.) 1950.

Hard ionizing x-rays were chosen as the injurious agent in the study of mammalian development, since the irradiation could be accurately timed and the selective response to the general action of the radiation might be interpreted as indicating intrinsic patterns of sensitivity in the organism.

Four hundred twenty newborn mice irradiated with x-rays of 250 kvp during intrauterine life were studied externally and by gross dissection. Treated embryos represented stages ranging from ½ to 13½ days after fertilization. The irradiated embryos and controls were hybrids of two pure strains (C57 black females were mated to NB strain males) and came from second

litters. Doses used were 200 r for a survey of all stages, while 300 and 400 r were used for comparisons at the last five stages.

Irradiation with 200 r before implantation and with 300 r at the 9½-day stage increased prenatal mortality in the early and late stages respectively. Considerable depression of the birth weight occurred after irradiation between the 8½- and the 13½-day stage, with the maximum approximately at 11 days.

With regard to two main types of effect—prenatal mortality and abnormality at birth—the mouse development seems to fall into three broad phases: 1. Between the ½- and the 4½-day stage there was a considerable incidence of early death, but normality among survivors at term was 98%. 2. Between the 6½- and the 13½-day stage there was no prenatal death but a high incidence of abnormalities at birth. 3. From the 14½-day stage to birth no prenatal death or visible abnormality was noted when doses of 300 r or less were used, but cataract, hydrocephalus, and cutaneous defects developed later in life.

Irradiation during the 6½- to the 13½-day phase revealed a definite pattern of critical periods in the formation of a variety of characters of the newborn. The external and visceral abnormalities which were produced with considerable frequency included microphthalmos, coloboma, narrow iris, vaulted cranium, snout-and-nostril abnormality, cranial blister, narrow head, open eyelids, spina bifida, small or imperforate anus, hydronephrosis and/or hydroureter, reduction in tail length, abnormalities of tail shape, overgrowth of feet (including polydactyly), digital reductions (including oligodactyly), and limb abnormalities. Each of the following abnormalities occurred in only one animal: pseudencephaly, hypospadias with persistence of cloaca, and situs inversus.

In some cases sensitivity occurred at the time of the visibly fastest degree of change in a primordium; e. g., the critical period for digital reduction corresponded to the time of growth of limb buds. In other cases, sensitivity was not predictable from the known facts of descriptive embryology. Russell concludes that there are both close similarities and striking differences between radiation-induced abnormalities and the effects of known genes.

Reid, New Brunswick, N. J.

Mitotic Stimulation of Amphibian Epidermis by Underlying Grafts of Central Nervous Tissue. Jane Overton, J. Exper. Zool. **115**:521 (Dec.) 1950.

Grafts of nerve tissue in the dorsal fin of Amblystoma opacum and Amblystoma punctatum larvae produced a fan-shaped enlargement of the fin by stimulating mitotic activity in the epidermis overlying the graft. The mitotic increase first appeared three days after operation, reached a peak in five to seven days, and then declined. At its height the mitotic index was about five times that of the control epidermis. This mitotic increase was localized. A local accumulation of basal-cell nuclei which accompanied the mitotic increase began to decrease in density after the fourth day. The local thickening of the epidermis over the graft reached a maximum on the fifth day.

No mitotic increase, basal-cell migration, epidermal thickening, or fin enlargement was produced by grafts of liver, muscle, cartilage, glass, paraffin, or injury to the host.

Grafts of nerve tissue killed by freezing or by freezing and drying, and even extracts of such tissues, produced a similiar, though less pronounced, effect than fresh nerve tissue. Grafts of hot-acetone-extracted nerve tissue had no effect.

With implantation of methylcholanthrene crystals the mitotic rate was high from the 6th through the 10th day. Extensive histological changes which occurred with the methylcholanthrene resulted in extrusion of the crystals. However, glass and paraffin, which were extruded in a similar manner, were not associated with the same mitotic increase.

The mitotic increase was most pronounced when the animals had been starved for two days, since mitotic figures were then rare in any part of the epidermis.

The mitotic increases for cord grafts, 5.2 mitoses per 1,000 nuclei; for feeding, 4.9 mitoses per 1,000 nuclei, and for methylcholanthrene, 3.9 mitoses per 1,000 nuclei, are all of the same order of magnitude.

Reid, New Brunswick, N. J.

Physiology and Biochemistry

REVASCULARIZATION OF BRAIN THROUGH ESTABLISHMENT OF CERVICAL ARTERIOVENOUS FISTULA: EFFECTS IN CHILDREN WITH MENTAL RETARDATION AND CONVULSIVE DISORDERS. C. S. BECK, C. F. MCKHANN and W. D. BELNAP, J. Pediat. **35**:317 (Sept.) 1949.

Beck and his associates point out that mental retardation, convulsive disorders, and sensory motor impairment are among the commonest of pediatric problems. The gliosis characteristic of these conditions has been found to interfere with the blood supply to cerebral tissue. They have attempted correction of the deficiency in circulation by production of an anastomosis between the common cartoid artery and the internal jugular vein, resulting in a redistribution and increase of blood flow to the brain. Eleven patients have been subjected to this procedure. Ten were children, ranging in age from 11 months to 14 years, who were mentally retarded, with or without a convulsive disorder. The eleventh was an adult, aged 38, with mental deterioration and left hemiplegia. The authors present the histories of 4 of the 11 patients. Although the postoperative follow-up observation is limited to one, three, and five months, benefit has been obvious. The remaining seven patients were operated on just prior to the writing of this report, and therefore their progress could not be evaluated. The authors believe this procedure represents the first successful attempt at correction of mental retardation on an organic basis. Complete restoration of normal function cannot be anticipated, but some return of function in the remaining viable neuronal tissue can be expected. The operation has proved safe. No difficulty has been encountered with reference to pulsating exophthalmos, increased intracranial pressure, or cardiac hypertrophy. The fistula could be closed should untoward results appear. The procedure is to be considered as a new approach to a problem, rather than as an acceptable and complete solution.

J. A. M. A.

DEPENDENCE OF NEUROMUSCULAR TRANSMISSION ON GLUCOSE. I. HAJDU and R. J. S. MCDOWALL, J. Physiol. **108**:502, 1949.

When the rat diaphragm is deprived of glucose, two varieties of block occur. The first can be related to the neuromuscular junction; the second would seem to be due to simple failure of the nerve elements. Since it has been shown by Feldberg (1945) that brain slices do not synthesize acetylcholine if deprived of glucose, and by Kahlson and MacIntosh (1939) that the perfused superior cervical ganglion fails to synthesize acetylcholine in the absence of glucose, it is suggested that the early block is due to failure of the synthesis of acetylcholine in the region of the nerve ending. This assumption is supported by the absence of the action of physostigmine after glucose block, the large change in chronaxia, and the absence of any effect on nerve within the period of the experiment. The exact nature of the subsequent block, which is the result of more prolonged exposure of the nerve to glucose insufficiency, was further investigated to determine whether it also could be related to acetylcholine, but without success. If it had been, it might have been expected that the onset of the block due to lack of glucose could be delayed temporarily by physostigmine, but this did not occur.

The facts given suggest that the mechanism of neuromuscular transmission may be linked to the energy mechanism in the muscle, and the muscle may thereby be protected against complete exhaustion of the carbohydrate stores necessary for its resting metabolism. It is probable that in the oxidation of pyruvic acid produced by the breakdown of glucose, thiamine, which von Muralt (1946) suggested is connected with humoral transmission, plays a part.

By the use of the block produced by lack of glucose, it becomes possible for the first time to study the pure muscle preparation without the use of curare or denervation, and the results already obtained in relation to chronaxia completely support the view of Rushton (1930) and further negate Lapicque's theory of isochronism.

THOMAS, Philadelphia.

THE EFFECT OF STIMULATION ON THE OPACITY OF A CRUSTACEAN NERVE TRUNK AND ITS RELATION TO FIBRE DIAMETER. D. K. HILL, J. Physiol. **111**:283, 1950.

The change in the opacity to white light of a crustacean nerve trunk following repetitive stimulation has been further investigated. The effect is measured by making photoelectric recordings of the intensity of light scattered by the nerve at right angles to the incident beam.

The chamber for holding the nerve was designed so that, in addition to the recording of the effect of stimulation, the change in opacity brought about by alterations in the composition of the solution surrounding the nerve could be investigated. It was found that the opacity of the nerve is very sensitive to changes in fiber diameter, brought about by altering the osmotic pressure of the solution. When the fibers swell, the opacity decreases; when they shrink, it increases.

The response to stimulation at 50 to 100 per second in normal sea water consists of an initial small increase of opacity, which is rather variable and may be absent, followed by a larger decrease, which reaches its maximum shortly after the end of the 5 to 10 per second period of stimulation, and then reverses slowly. At its peak the decrease in the intensity of the scattered light, due to stimulation at 50 per second for 10 seconds is about 1 part in 100 of the resting intensity. Recovery appears to be complete in about 10 to 15 minutes. It is shown that the latter phase of decreased opacity can probably be attributed to an increase in diameter of the individual nerve fibers, and it is calculated that this increase lies between 0.0009 and 0.009 μ for 500 impulses.

The initial increase of opacity due to stimulation can be greatly exaggerated by slight dilution of the solution surrounding the nerve. The reason for this is not clear.

The dependence of opacity upon the fiber size has been made use of in studying the permeability of the fiber membrane to certain solutes. There is evidence which suggests that the permeability to sodium ions can be increased by removing calcium from the solution, and decreased by adding an excess.

Thomas, Philadelphia.

Torulosis of the Central Nervous System. W. H. Mosberg and J. A. Alvarex-DeChoudens, Lancet **1**:1259 (June 9) 1951.

The authors attempted to grow Cryptococcus neoformans in culture media of varying pH and found that the more acid the medium, the greater the growth response, and the more alkaline the medium, the weaker the growth response. They also found that incubating the organisms at 40 C. for a sufficient length of time retarded their growth. These facts suggest that human cryptococcosis of the central nervous system should be treated by a combination of hyperthermia and alkalization.

Madow, Philadelphia.

Metabolic Disorders in Head Injury. G. Higgins, Walpole Lewin, J. R. P. O'Brien, and W. H. Taylor, Lancet **1**:1295 (June 16) 1951.

The authors report six cases of severe head injury with an unusual biochemical complication characterized by the presence of a high plasma chloride ion concentration in the absence of significant excretion of the ion in the urine. This condition had been previously described in four groups of diseases, including disturbances in acid-base balance, gastrointestinal hemorrhage, cerebral damage, and sulfathiazole poisoning. The authors believe that the essential mechanism is the inability of the kidney to excrete chloride ion. Therefore, it would seem unwise, if a patient has hyperchloremia and hypochloruria, to give sodium chloride until either the plasma chloride level falls to normal or the chloride ion appears in the urine in amounts greater than 1 gm. per liter.

Madow, Philadelphia.

The Plantar Reflex in Healthy Persons. F. Morgenthaler, Schweiz. Arch. Neurol. u. Psychiat. **62**:199, 1948.

Two hundred healthy students, aged 14 to 18 years, served as subjects for this study. The outer margin of the sole of each foot was stroked from heel to ball, first with the handle of a reflex hammer, and then with the point of a needle. Comparison of the author's observations with those reported by others indicated that the usual clinical methods of stimulation yielded results equally as reliable as those obtained with a rigidly standardized technique. In about 10% of Morgenthaler's subjects there was no response to plantar stimulation, the percentage being slightly lower when a sharp stimulus was employed. Extension of the great toe was observed in 2% when a sharp stimulus was used and in 1.5% when the stimulus was blunt, but it was

never associated with spreading of the other toes. Extension of all toes was about four times as frequent as extension of the great toe with flexion of the remaining toes. The higher incidence of extension of the great toe reported by H. A. Davidson (Plantar Reflexes in Normal Adults Arch. Neurol. & Psychiat. **26**:1027-1037 [Nov.] 1931) was attributed to the fact that he stimulated the heel and the ball of the foot separately, the tendency to extension being greater when the ball alone is stimulated. Extension of the great toe, consequently, assumes greater significance when the stimulus is confined to the region of the heel. Spreading of the toes was noted by Morgenthaler in somewhat less than 10% of his subjects when he used a sharp stimulus and in only 5% when the stimulus was blunt.

Extension of the great toe was observed about three times as frequently on one side only as on the two sides. Spreading of the toes was a bilateral phenomenon in only 1 of 10 trials. Flexion of the entire lower limb was observed in approximately one-third of the cases, and was then seldom pronounced. The only movement of the foot observed to accompany extension of the toes was one of dorsal flexion. Morgenthaler expresses the belief that extension of the big toe, when not associated with spreading of the other toes, is consistent with an intact motor system.

Daniels, Denver.

Neuropathology

Diffuse Angiectasis of the Cerebral Meninges of the Newborn Infant. Edith L. Potter, Arch. Path. **46**:87, 1948.

The author has searched the literature and has failed to find descriptions of vascular abnormalities generalized over the surface of the brain in any age group similar to those which she reports in this article. The present report concerns three newborn infants whose meningeal vessels showed remarkable changes in gross appearance. In each instance there was also an abnormality of the heart.

The vessels of the meninges in two of the infants were almost identical in appearance. Over the entire surface of the cerebrum and the cerebellum these vessels were of fairly uniform size and exhibited a great increase in number and tortuosity. They formed a scroll-like pattern, and their many convolutions produced a generalized tangled mass over the exterior of the brain. They had no connection with the vessels of the brain or those of the dura, and all were confined to the leptomeninges. In the third infant the appearance of the meningeal vessels was somewhat different, although here, too, a scroll-like tortuosity was the principal abnormality. The increase in the total number of vessels was somewhat less striking than in the other infants, and the proximal portions were of considerably greater caliber than were the distal branches.

As already mentioned, the three infants had an associated abnormality of the heart. In two it consisted of generalized hypertrophy. The size of the chambers was abnormally great and the muscle was increased in thickness, but the valves and the great vessels leading from the heart were normal. The third infant had only slight enlargement of the heart, but the left innominate vein entered the left atrium, instead of joining the right innominate vein to form the superior vena cava. This infant also had an abnormality of the liver consisting of the presence of numerous superficial veins, lying immediately beneath the capsule, diffuse dilatation of the veins in the center of the lobules, and a moderate increase in periportal connective tissue.

The author comments on the coincidence of the abnormality of the cerebral vessels in association with the abnormalities of cardiac development. She speculates that the heart might be hypertrophied in order to supply the increased vascular bed in the meninges. She also suggests that the hypertrophy of the heart may have caused sufficient increase in cardiac output and pressure to be responsible for hyperdevelopment of the meningeal vessels.

The fact that this condition is not recognized in later life suggests that it may be incompatible with continued existence and that all those affected die in early infancy.

Winkelman, Philadelphia.

Intracranial Vascular Lesions in Late Rheumatic Heart Disease. John Denst and Karl T. Neubuerger, Arch. Path. **46**:191, 1948.

Denst and Neubuerger, spurred on by the work of Bruetsch on what he called rheumatic disease of the brain, turned their attention to the changes that were present in nonpsychotic

patients with a history of rheumatic fever and rheumatic heart disease. In a series of 688 consecutive autopsies, rheumatic heart disease was noted in 45 patients older than 25. The brain was adequately examined in 14 of these patients, in 9 of whom it showed significant vascular changes.

The authors summarize the vascular changes observed in their series as follows: The vessels chiefly involved were the small, medium-sized, and larger basal arteries, as well as the veins of the leptomeninges. In three cases the lumen of the large vessel contained, but was not completely obstructed by, a spongy, polypoid thrombotic mass made up predominately of fibrin and covered by a layer of flat endothelial cells. Thrombi of this type sometimes showed admixture of erythrocytes and small collections of foam cells. Unlike the thrombi typically seen in other conditions, these resembled the cardiac valvular vegetations that are present in rheumatic endocarditis.

The other principal lesions observed were various forms of thrombosis, endarteritic proliferation, alteration of the elastic membranes, and fibrosis of media and adventitia.

The histologic picture, as a rule, was thought to be sufficiently characteristic to permit differentiation from other vascular diseases that occur in the same location. Parenchymal changes in the brain secondary to the vascular processes are identical with those produced by other vascular diseases. Focal neurologic signs may occur, but the authors are convinced that there is little evidence to show that the lesions described by them could form the anatomic basis for a psychotic syndrome. They quote Moersch in a recent discussion of Bruetsch's last paper, "It is not known how numerous or how extensive lesions in the brain must be for the production of mental symptoms."

WINKELMAN, Philadelphia.

MYOCARDIAL CHANGES IN POLIOMYELITIS. VERA B. DOLGOPOL and MARY D. CRAGAN, Arch. Path. **46**:*202*, 1948.

The microscopic evidence of myocarditis in poliomyelitis was first reported in 1941 by Larson, who encountered this condition in 2 of 12 necropsies in cases of that disease. The two cases were described in detail two years later by Dublin and Larson. Dolgopol and Cragan found focal myocarditis in 16 of 92 cases of poliomyelitis. The incidence of myocarditis in 45 cases in which multiple sections from each heart were available was 26.6%. Cardiac failure was the immediate cause of death in at least four cases.

Electrocardiographic studies of patients with poliomyelitis who showed evidence of cardiac failure was reported in Argentina in 1943. The authors of this article, (Battro, A.; Cibils Aguirre, R., and Mendy, J. C.: Rev. argent. cardiol. **11**:185 [July-Aug.] 1944) found transient myocarditis in 4 of 20 patients in the acute stage of poliomyelitis and none of 18 patients in the chronic stage. Morrow had observed abnormal electrocardiographic tracings of some convalescent patients in the Knickerbocker Hospital in New York.

In most of the cases myocarditis was observed in the second and fifth days of illness. Pneumonia and other evidence of pulmonary inflammation were absent in one-half of the 16 cases. Myocardial interstitial edema was present in most of the 92 cases. Intrasarcolemmal fragmentation of myocardial fibers, with preservation of striation in the retracted fibers and collapse of the sarcolemmal sheath, was seen in many cases in which no myocarditis was found and in a few cases of myocarditis. The authors conclude that the myocarditis may in some cases be regarded as the immediate cause of death.

WINKELMAN, Philadelphia.

FORMATION OF HEMOSIDERIN AND HEMATOIDIN AFTER TRAUMATIC AND SPONTANEOUS CEREBRAL HEMORRHAGES. GEORGE STRASSMANN, Arch. Path. **47**:205, 1949.

Strassmann attempts to determine the exact time at which the histiocytes containing hemosiderin and/or hematoidin appear after traumatic and spontaneous cerebral hemorrhages. Experiments were made with mice and the results compared with autopsy observations in man. The author found that hemosiderin appeared earlier after blood was injected into animal tissues or after injuries of the brains of mice than after cerebral hemorrhage in man. He concludes that it is probable that scarcity of available histiocytes and their slow activation explain the late formation of the human blood pigments. The author found that histiocytes with hemosiderin appear on the fifth or sixth day after cerebral injuries and hemorrhage, and that histiocytes with hematoidin become visible after 10 to 14 days.

WINKELMAN, Philadelphia.

Psychiatry and Psychopathology

Acute Alcoholism in Mental Patients Treated with Insulin. S. J. Tillim, Am. J. Psychiat. **104**:576 (March) 1948.

Tillim says that when alcohol addicts are admitted to hospitals they either are intoxicated or present after-effects of intoxication, involving psychiatric, nervous, and nutritional disorders. Patients may exhibit mental clouding to the point of delirium with delusions and hallucinations; nervousness, displayed in tremor; ataxia and restlessness, and nutritional defects, manifested by dehydration, refusal or inability to accept nourishment, and signs of avitaminosis. Prompt induction of rest and sleep and measures to correct the nutritional deficiency are indicated. Insulin-induced hypoglycemic reactions are preeminently effective in providing the rest and sleep and in conditioning the patient for the acceptance of nourishment without recourse to force or parenteral administration. Favorable results from the use of insulin in the medical treatment of alcoholism have been reported by others. The author presents seven cases which provide additional evidence on the efficacy of insulin therapy. He concludes that this method is the most rapid in restoring normal mentation and physical health and that it is more specific in purpose than any other method presently in vogue.

J. A. M. A.

Toxic Psychosis Due to Overdosage with Prophenpyridamine (Trimeton). S. Waldman and L. Pelner, J. A. M. A. **143**:1334 (Aug. 12) 1950.

Waldman and Pelner report two instances of toxic psychosis with recovery due to overdosage with prophenpyridamine ("trimeton"). Prophenpyridamine in toxic doses has an atropine-like effect. (Atropine is also antihistaminic in character.) It is again pointed out that the margin of safety of prophenpyridamine is relatively great and that its toxicity is relatively low.

Alpers, Philadelphia.

Personality Structure in Relation to Tetraethylthiuramdisulfide (Antabuse ®) Therapy of Alcoholism. Capt. P. W. Dale and F. G. Ebaugh, J. A. M. A. **146**:314 (May 26) 1951.

Tetraethylthiuramdisulfide creates a biochemical intolerance to alcohol. Of even greater importance in many patients, depending upon the structure of their personality, is the appearance of psychologic reactions to tetraethylthiuramdisulfide therapy. This paper is a preliminary report by Dale and Ebaugh, after one year's experience with 60 cases, of a study of the emotional reactions of the alcoholic patient to tetraethylthiuramdisulfide therapy. The authors found that what amounts to the forceful withdrawal of alcohol by use of tetraethylthiuramdisulfide may result in hypochondriacal states, in increased hostility, either objectively directed or introjected, in anxiety, in other habituations, in "crusadism," or in no apparent personality changes, depending upon the personality structure of the patient. The administration of this drug should therefore be accompanied by other therapeutic measures, particularly psychotherapy, so as to avoid perpetuating the hypochondriacal state, handle the resulting hostility and anxiety, and insure some measure of insight.

Patients with reactive alcoholism and those with essential alcoholism do well under tetraethylthiuramdisulfide therapy, while the patient with a character neurosis, the patient with periodic alcoholism, and the patient with alcoholism as a symptom of an underlying major psychosis do poorly.

Tetraethylthiuramdisulfide seems to find its greatest place in that largest of all diagnostic groups, the patient with essential alcoholism. Treatment of this group puts less strain on existing medical faculties than did former approaches and appears to be equally, or more, successful.

Alpers, Philadelphia.

Alopecia Areata as Conversion Symptom. R. E. Peck, J. M. A. Georgia **37**:226 (June) 1948.

Peck cites four cases in which alopecia areata occurred as the initial symptom of a generalized neurosis. In two cases the onset of alopecia areata was associated with sudden and overwhelm-

ing fright, and in the other two, with the onset of chronic anxiety. In one the mechanism seems clearly that of a conversion symptom. The same mechanism may be postulated in the other three cases, as conversion symptoms are frequently seen in the ordinary traumatic anxiety neurosis and anxiety hysteria.

J. A. M. A.

EFFECT OF DIRECT INTERRUPTED ELECTRO-SHOCK ON EXPERIMENTAL NEUROSES. J. H. MASSERMAN, A. ARIEFF, C. PECHTEL, and H. KLEHR, J. Nerv. & Ment. Dis. **112**:384 (Nov.) 1950.

The authors investigated the effects of square-wave (nonsinusoidal) unidirectional impulses in abolishing neurotic patterns created by motivational conflicts. Cats trained to execute complex acts to obtain food were subjected to shocks or air blasts as they attempted to get food. "Hunger-fear" conflicts resulted in "neurotic" disturbances, such as startle responses or inhibition of activity. The cats successfully trained to obtain food were subjected to convulsive seizures by square-wave unidirectional current. This produced milder convulsions and less postconvulsive confusion than sinusoidal current. After the electroshock treatment, the animals were less resistive to entering the apparatus and had fewer startle reactions, but showed inertia, repetitive activity and general inertia. However, ultimately the animals showed a persistent "neurotic" pattern and impaired capacity for retraining after convulsive therapy.

BERLIN, New York.

REPORT ON THE CURRENT STATUS OF AN ATTEMPT TO CORRELATE ABNORMALITY OF DISTRIBUTION OF ONE BRAIN ENZYME WITH MENTAL DYSFUNCTION. W. ASHBY, J. Nerv. & Ment. Dis. **112**:425 (Nov.) 1950.

Ashby studied the distribution of carbonic anhydrase in the central nervous system of 145 human subjects and 300 animals. There appears to be a pattern of quantitative distribution of the enzyme corresponding to function, so that the subcortical white matter has about five times the carbonic anhydrase of the cauda equina. In the course of development of the nervous system, the appearance of carbonic anhydrase is correlated with the onset of functional activity. Within the cerebral cortex the pattern is such that the temporal pole contains less than the frontal or the occipital pole. In animals with a poorly developed cerebral cortex, the thalamus or cerebellum may have a higher enzyme concentration than the cerebral cortex. In cases of syphilis, tuberculous meningitis, and arteriosclerosis there was a striking depression of the enzyme in the parietal lobes.

BERLIN, New York.

BASIC MENTAL CONCEPTS: THEIR CLINICAL AND THEORETICAL VALUE. EDWARD GLOVER, Psychoanalyt. Quart. **16**:482 (Oct.) 1947.

Glover contends that the basic concepts on which psychoanalytic theory is founded can, and should, be used as a discipline to control all hypothetical reconstructions and etiological theories that cannot be directly verified by clinical psychoanalysis. Since clinical analysis is not possible until the infant can apprehend the meaning of spoken interpretations, this means that all theories and reconstructions bearing on at least the first two years of life should be subject to this discipline.

The author states that the greatest difficulty in making plausible reconstructions of early development lies in the fact that while we cannot do without the concept of organized structure, the earlier the stage to which we seek to apply this concept, the more violence it does to our reconstructions. No doubt it is possible to underestimate, as well as to overestimate, the complexity of organization of early psychical life, but in Glover's opinion the greater scientific danger lies in overestimation. For this reason, he suggests applying the term "embryonic" to those earlier dynamic stages of development that cover the first two years of life. If, by adopting this usage, we occasionally do less than justice to the precocity of the exceptional infant, at any rate we avoid the danger of accepting fantastic reconstructions that bring metapsychology into merited disrepute.

Glover believes that we must treat with the utmost reserve reconstructions that postulate a functional identity between the first and the third year. Fortunately, this pitfall can be avoided,

according to the author, if we submit all reconstructions to the most meticulous scrutiny, using for this purpose the basic mental concepts left us as a scientific heritage by Freud.

WERMUTH, Philadelphia.

SOMATIC INVESTIGATIONS IN SCHIZOPHRENICS: SCHIZOPHRENIA AND ANOREXIA NERVOSA. O. LINGJAERDE, Nord. med. **41**:215 (Feb. 4) 1949.

Lingjaerde says that the picture in the active phase of schizophrenia resembles that of anorexia nervosa: loss of weight, variable temperature and pulse rate curves, varying sedimentation reaction, constipation, amenorrhea, low blood pressure, low basal metabolic rate, pathologic urobilinuria, and ketonuria. Necropsy reveals organic atrophy, like that in long-continued inanition. The increased urobilin in the urine, associated with ketonuria, is primarily due to carbohydrate deficiency. Disinclination for food is characteristic of the active phase of schizophrenia. In anorexia nervosa this disinclination for food is a major symptom. Refusal to eat and the resulting symptoms are regarded as an important pathogenic factor, at least in a large number of cases of schizophrenia. The author explains the dissociation symptoms of schizophrenia as the outcome of a dynamic-energetic weakening of the ego which occurs in predisposed persons in the active phase, when the ability to concentrate is weakened and consciousness is reduced. In this weakening of the ego, malnutrition and hepatic insufficiency, together with prolonged isolation, introversion, inactivity, and more accidental complications of an infectious or toxic kind, play an important part. The effect of malnutrition is heightened by the deficient utilization of carbohydrates.

J. A. M. A.

Diseases of the Spinal Cord

ACUTE ANTERIOR POLIOMYELITIS IN PREGNANCY. E. S. TAYLOR and J. M. SIMMONS JR., Am. J. Obst. & Gynec. **56**:143 (July) 1948.

Taylor and Simmons found that during the 1946 epidemic of poliomyelitis in Colorado the pregnant woman was twice as vulnerable to the virus disease as the nonpregnant woman of the same age group. Women in all months of pregnancy were equally susceptible to poliomyelitis. During the first two trimesters the prognosis for recovery is excellent. Poliomyelitis acquired during the last trimester carries a serious prognosis with respect to survival of the mother or escape from severe permanent paralysis. Estrogen and progesterone may be protective to a victim of poliomyelitis early in pregnancy. This is not true in the last trimester. The virus does not pass the placental barrier. All children born of mothers infected during this epidemic have been free from congenital disease. Management of pregnancy accompanied with acute poliomyelitis in the last trimester of pregnancy is a challenging problem. In the acutely ill patients, Caesarean section seems unreasonable. Poliomyelitis had no ill effects on the progress of labor except that it necessitated an occasional forceps operation.

J. A. M. A.

METABOLISM OF CALCIUM IN PATIENTS WITH SPINAL CORD INJURIES. L. W. FREEMAN, Ann. Surg. **129**:177 (Feb.) 1949.

Freeman directs attention to the high incidence of calculi of the urinary tract in patients with paraplegia. The report is based on clinical observations, particularly with regard to the calcium metabolism, made on over 700 men (aged 18 to 50) who had suffered injury to the spinal cord during and shortly after World War II. The incidence of calculi of the urinary tract during prolonged recumbency was found to be between 23 and 35%. The author feels that while considerable emphasis has been placed on the role of recumbency, insufficient stress has been placed on weight bearing. It was found that ambulation reduces the incidence of calculi to such a degree that the presence of a calculus can be taken as an indication of the failure to ambulate sufficiently. Neurogenic ossifying fibromyositis is discussed as a reflection of the aberrant state of calcium metabolism in the presence of infectious and inflammatory processes.

J. A. M. A.

POLIOMYELITIS: I. BULBAR POLIOMYELITIS; A NEUROPHYSIOLOGICAL INTERPRETATION OF CLINICOPATHOLOGICAL FINDINGS. JOSEPH R. BROWN and A. B. BAKER, J. Nerv. & Ment. Dis. **1**:54 (Jan.) 1949.

The author reports clinical and pathologic findings in five groups of cases of bulbar poliomyelitis based on the predominant area of involvement: (1) cranial nerve nuclei, (2) respiratory center, (3) circulatory center, (4) encephalitic, and (5) combined bulbar-cervicothoracic. Involvement of the cranial nerve nuclei is not threatening to life except that impairment of the 9th and 10th nerves warns of possible progression to more vital areas and is an indication for an elective tracheotomy and the use of oxygen.

Destructive lesions were observed in the ventral reticular substance at the level of the inferior olivary nucleus in patients with central respiratory failure and in the dorsal reticular substance at the same level in patients with central circulatory failure. These findings confirm in humans the experimental data known for these respective centers in cats. Encephalitic symptoms were sometimes remedied by adequate oxygenation and were then attributed to cerebral anoxia rather than to viral invasion.

In 59 cases of bulbar poliomyelitis, there were 26 deaths, due mainly to central respiratory or circulatory failure. If the spinal cord was also involved so as to produce peripheral respiratory failure, the prognosis was much more serious.

The following guides to therapy are recommended: early elective tracheotomy and early closure after the opening is not needed, administration of up to 40% oxygen under positive pressure for pulmonary edema, adequate humidification, arterial oxygen determinations, turning of the patient to prevent hypostasis and thrombophlebitis, nasal feedings, prophylactic use of penicillin, avoidance of sedatives and the use of stimulants, and unceasing watchfulness of the patient and of the mechanical devices on the part of the physicians and special nurses.

FARMER, Philadelphia.

POLIOMYELITIS IN FAMILIES ATTACKED BY DISEASE: II. THE PRESENCE, APPEARANCE AND PERSISTENCE OF NEUTRALIZING ANTIBODIES. H. A. WENNER and W. A. TANNER, Pediatrics **2**:190 (Aug.) 1948.

Wenner and Tanner pointed out in a previous paper that whenever poliomyelitis appears in certain households all the children, and sometimes adult members, have poliomyelitis. Frequently the disease is so mild that its existence can be determined only by finding poliomyelitis virus in the stool or, as is less readily the case, in the oropharynx. If one considers the differences in clinical response among all the members in a family in which poliomyelitis virus is widely seeded, the question arises concerning the appearance and persistence of neutralizing antibodies in these patients. In 1946 members of households were sampled to delineate the distribution of poliomyelitis virus within family units in which poliomyelitis appeared. Several members in these family units were selected for inclusion in the present study. Five of the six patients studied had poliomyelitis, and the sixth was a familial contact. It was found that neutralizing antibodies do appear in the serums of patients convalescent from poliomyelitis. Neutralizing antibodies, as a rule, appeared during the first 10 days of illness. There is little, if any, fall in titer during the ensuing year. It was also evident that in some patients ill with poliomyelitis the neutralizing antibody does not reach a high level. The authors cite observations on a paralyzed patient to prove this.

J. A. M. A.

VIRUS ISOLATED FROM PATIENTS DIAGNOSED AS NON-PARALYTIC POLIOMYELITIS OR ASEPTIC MENINGITIS. J. L. MELNICK, E. W. SHAW and E. C. CURNEN, Proc. Soc. Exper. Biol. & Med. **71**:344, 1949.

Melnick and associates report the isolation of a filtrable virus from the feces of patients whose condition was diagnosed as either nonparalytic poliomyelitis or aseptic meningitis and from two patients with "fever of unknown origin." The agent is similar to that reported by Dalldorf and Sickles in producing paralysis with myositis in newborn mice. The recovery of virus was correlated with the appearance of neutralizing antibodies in the patients' serum. At least two immunologic types of the virus exist. The virus was widespread in this country

during the summer of 1948, having also been isolated from the sewage of a number of cities and from flies collected in widely separated areas. Subclinical infection may be produced in chimpanzees by oral administration of the virus. A laboratory worker has been accidentally infected with the virus.

J. A. M. A.

Epidemiological Significance of Behavior of Poliomyelitis in Warmer Climates. W. L. Aycock, Hawaii M. J. **7**:461 (July-Aug.) 1948.

According to Aycock the spread of the virus of poliomyelitis is extensive and is the result of ordinary, unavoidable, and probably irreducible contact. Infection with this virus is preponderantly benign, the one serious sequel of infection, paralysis, occurring in only a small fraction of persons exposed. In the tropics the evidence indicates that in terms of parasitism adaptation between virus and host is even more nearly balanced. Widespread exposure to the virus, more frequently during the persistence of equally widespread maternal immunity, apparently results in more frequent modified infection, but still with propagation of virus, with resultant active immunity to be passed on to the offspring for repetition of the cycle. Thus, in warm climates a high degree of commensalism with the virus has been attained. In poliomyelitis there are a number of selectivities seen in the occurrence of paralytic disease in the few of the many exposed to the virus which indicate that this "complication" of the ordinarily subclinical infection is determined primarily not by circumstances of exposure to the virus but by autarceologic influences. The mechanism through which a lower incidence of paralysis occurs in a warmer climate seems to be the operation in nature of the principle of variolation, rather than the principle of vaccination. It is suggested that the virus of poliomyelitis requires host conditions of warm weather or warm climate both for disease production and for multiplication, and hence propagation. Such a conception, under which this virus could be active for only a brief part of the year in more temperate climates and throughout the year in warmer climates, could account for the more rapid and extensive dissemination of the virus in warmer climates.

J. A. M. A.

Laterally Placed Cervical Discs. M. Jefferson, Lancet **1**:129 (Jan. 20) 1951.

Jefferson states that there is now plentiful evidence that lateral rupture of cervical disk is, in fact, more, rather than less, common than central protrusion and that brachial neuralgia of radicular type is, accordingly, more usually encountered than the syndromes of spinal cord compression.

He reports 12 cases with disturbance of cervical nerve roots due to ruptured disk, in 4 of which the diagnosis was verified at operation, in 2 confirmed myelographically, and in 6 made on clinical grounds alone. The nerve root involved was the seventh cervical alone in seven cases and the sixth cervical alone in four cases. In the one case of a lesion of the first thoracic nerve root there was simultaneous compression of the seventh cervical root by a second disk. The location could be established clinically on the basis of the distribution of the arm pain and the distal paresthesias. Roentgenograms of the cervical vertebrae showed changes coinciding with the proper root level in only six cases. Treatment included immobilization with a plaster cast, which the author felt was most generally useful, and operation, which should be reserved for cases in which symptoms are of long duration and resist more conservative measures.

Madow, Philadelphia.

Poliomyelitis and Gastric Acidity. Phyllis G. Ashworth, M. J. Australia **1**:793 (June 26) 1948.

Ashworth investigated the gastric acidity of persons over 10 years of age who contracted poliomyelitis in the 1945-1946 epidemic. Examinations were made approximately one year after the onset of disease, during the summer and autumn of 1946-1947. Of the 228 survivors over 10 years old, 91 were investigated. No evidence was found that gastric acidity of the population with poliomyelitis has a different distribution from that of a normal population.

J. A. M. A.

News and Comment

NATIONAL INSTITUTE OF NEUROLOGICAL DISEASES AND BLINDNESS

The National Institute of Neurological Diseases and Blindness, under Dr. Pearce Bailey, Director, now has funds available for the support of research grants-in-aid, research fellowships, and traineeships in rehabilitation.

Research grants-in-aid are awarded to nonfederal institutions for the support of research projects submitted by qualified investigators in their particular fields of interest. Research fellowships will be awarded to promising students and scholars for their support in their predoctoral and postdoctoral research training. The Institute has limited funds for training of various professional personnel in methods of rehabilitation so that they can later assume a teaching function and become the nuclei of rehabilitation groups throughout the country.

Further information and applications for grants and fellowship may be obtained from Dr. Frederick L. Stone, Chief of Extramural Programs, National Institute of Neurological Diseases and Blindness, Bethesda 14, Md.

ASSOCIATION FOR RESEARCH IN NERVOUS AND MENTAL DISEASE

At the annual meeting of the Association for Research in Nervous and Mental Disease, held in New York on Dec. 14-15, 1951, these officers were elected for 1952: president, Dr. H. Houston Merritt; first vice-president, Dr. Robert F. Loeb; second vice-president, Dr. Charles D. Aring; secretary-treasurer, Dr. Clarence C. Hare; assistant secretary, Dr. Rollo J. Masselink. Two additional trustees, Dr. Merritt and Dr. Hare, were elected to enlarge the board of trustees from five to seven.

The subject for the 1952 meeting will be "Metabolic and Toxic Diseases of the Nervous System."

DIAGNOSTIC SERVICE FOR NEUROPATHOLOGIC STUDIES OF CEREBRAL PALSY

St. Christopher's Hospital for Children, in cooperation with the United Cerebral Palsy Fund and the department of pediatrics of the Temple University School of Medicine, announces the establishment of a diagnostic service for neuropathologic studies of cerebral palsy.

The facilities of any single institution for investigation of neuropathologic problems are limited by the relatively small number of autopsies performed on children with neurologic disorders and by the inaccessibility of facilities for detailed histologic examination of the central nervous system. This new service, under the direction of Dr. J. B. Arey and Dr. W. E. Nelson, with Dr. Ernest Spiegel as consulting neuropathologist, was formed to make these facilities available to more physicians and hospitals and to correlate the clinical course and pathologic findings in children in whom (1) a disease of the central nervous system is suspected, or for whom (2) the diagnosis of cerebral palsy has been entertained or established.

The institution submitting a clinical history and the brain from such a patient will receive a detailed report, together with a pertinent bibliography and representative histologic sections within six months after the specimen is received. Transportation costs and suitable containers will be furnished upon application to Dr. James B. Arey, St. Christopher's Hospital for Children, 2600 North Lawrence St., Philadelphia 33.

CENTRAL NEUROPSYCHIATRIC ASSOCIATION

The Central Neuropsychiatric Association met in St. Paul and Minneapolis, Oct. 19 and 20, 1951. The Minnesota Society of Neurology and Psychiatry were hosts, and the scientific program was prepared under their auspices.

The next meeting will take place in Nashville, Tenn. during Oct. 1952.

The officers for the coming year are Dr. Raymond Walther Waggoner, president; Dr. Lee M. Eaton, vice president; Dr. Hamilton Ford, secretary-treasurer, and Dr. Frank Luton, counselor.

AMERICAN ACADEMY OF FORENSIC SCIENCES

The fourth annual meeting will be held March 6, 7, and 8, 1952, at the Biltmore Hotel, Atlanta. There will be general sessions and special section meetings on forensic pathology, forensic toxicology, and forensic psychiatry. All persons interested are urged to attend these meetings. Prof. Ralph Turner, Michigan State College, East Lansing, Mich., is secretary.

The complete proceedings of the third meeting of the Academy are in the hands of the printer. Orders for the proceedings may be filed with Prof. Ralph F. Turner, Department of Police Administration, Michigan State College, East Lansing, Mich. The price is $8 per copy.

Obituaries

DONALD SNELL McEACHERN, M.D.

1904-1951

Donald McEachern died in the prime of life. It happened one afternoon with great suddenness, on a day when he was working quietly and Mrs. McEachern was away at Lake Memphremagog supervising the building of their country house.

Thus, the Faculty has lost an able teacher; the Montreal Neurological Institute, a skilled neurologist and investigator; his colleagues, a cherished friend; the sick, a wise physician.

His academic record was brilliant from the start. Although he graduated in medicine from the University of Manitoba when only 21, he took the Chown Prize for the highest aggregate standing. At the same time he was recognized as one of the university's best hockey players, and, as the result of his collateral reading, he had come to be a devout, though distant, disciple of William Osler.

After graduation he spent two years as intern in Winnipeg and then three years in the Johns Hopkins Hospital. He was drawn toward Baltimore, as he admitted afterward, by the spell that Osler had cast upon him.

Subsequently, as fellow in medicine of the National Research Council (Washington, D. C.), he was able to spend a year in biochemical research with Professor Myerhoff, at Heidelberg, and a year in neurophysiology with Sir Henry Dale, in London. After this he returned to the department of cardiology at the Johns Hopkins University.

At this time, in response to an invitation from McGill University, he decided to enter the field of neurology and to join the newly formed department of neurology and neurosurgery; so he came to Montreal to work for a few months under Prof. Colin Russel. That was in 1934, and when the Montreal Neurological Institute was opened he was appointed associate neurologist and was given leave of absence so that he could return to London for a year of clinical neurological experience at the National Hospital.

McEachern was a man of action, and there were reasons for his eagerness to return to London that his colleagues in Montreal had not suspected. When he arrived in Southampton, he telephoned to a charming Winnipeg friend, Corinne Irwin, who was at that time employed as a newspaper reporter in London. Within 24 hours they were engaged. Three days later they were married. No "whirlwind courtship" has ever been blessed by happier sequel than that one. In addition to Mrs. McEachern, he is survived by a daughter, Gail, and a son, John.

Returning to Montreal, he founded and directed the laboratory of neurochemistry in the Montreal Neurological Institute. In 1945, upon the retirement of Dr. Russel, Donald McEachern succeeded to his post as chief neurologist of the Institute and neurologist to the Royal Victoria Hospital. He served as lieutenant colonel in the Royal Canadian Army Medical Corps. He became associate professor of neurology, and consulting neurologist at Queen Mary Veterans' Hospital. He was this year president of the Canadian Neurological Society.

The series of eighty-seven publications on scientific subjects that is found in his bibliography shows a remarkably logical evolution of interest from studies of thyroid and of the physiology of heart muscle to muscle chemistry. Then, leaving the field of cardiology for neurology, he turned to myasthenia gravis, the circulation of the brain, and acetylcholine in the epileptic brain. Finally, he returned to his early interest in muscle physiology, and not long before his death he had demonstrated clearly that certain neuromuscular disorders could be treated successfully by cortisone. Many sufferers from these diseases owe their life to him today.

To us, his fellow-workers, the loss of our companion is hard to bear, but we know that it is still harder for his family and we give them our heartfelt sympathy. He lived his life with due consideration for those he loved. He took his proper place in the community.

In medicine and science, as in life, every man who sees the goal contributes what he can according to his strength. He runs in a never-ending relay race. Donald McEachern has handed on his baton to the man who is swift enough to carry it. He ran a good race, and he broke the tape with honor.

WILDER PENFIELD, M.D.